U.S. DEPARTMENT OF AGRICULTURE

NATIONAL CONFERENCE ON FOOD SAFETY RESEARCH

Thursday, November 12, 1998

8:00 a.m.

Ramada Plaza Old Town
Lee Ballroom
901 North Fairfax Street
Alexandria, Virginia

C O N T E N T S

C O N T E N T S(Cont'd.)

P R O C E E D I N G S

SESSION I

Opening Comment & Introduction of

Secretary Glickman

Dr. KENNEDY: My name is Eileen Kennedy. I see a lot of familiar faces in the audience. I am Deputy Undersecretary for Research Education and Economics. I am delighted to welcome all of you to USDA's first annual food safety research conference. And I have a very pleasurable task this morning, which is introducing our Undersecretary for Research, Education and Economics, Dr. Miley Gonzalez.

A little over a year ago I did not know Miley, but his words preceded him. I was thinking about this last night. My children always say to me, "Never tell jokes, Mom," because they think they're very obtuse and no one gets the point. I was thinking of a lot of witty moments with Miley, but I'll be a little bit more serious.

Before I ever met Miley, I had the opportunity to actually read his statement as he was going before the Senate Confirmation. And I'm a pack rat, so I actually had the material at home and I pulled it out. And I did remember pretty correctly, there was a statement he made when he went before the Senate wherein outlining his priorities.

And I'd like to read this quote, an effort "To provide a forum to address the concerns of producers, scientists, educators, and other stake holders, and to put forward a clear articulation of a vision for the future."

I think Miley has already done that in the little over a year he's been with the department. I think this conference on food safety is a clear indication that the Undersecretary meant what he said to the Senate. And the next two days will serve a whole variety of purposes.

I'm looking forward to not only a very substantive set of presentations from the presenters and panelists we have coming forward, but I think an even livelier discussion across the participants represented in this audience. And I think we all agree that this is vitally important to what we in USDA want to do to ensure a safer food supply. And this is one of many of the hallmarks of Dr. Gonzalez in not only talking about the substantive issues, but providing a forum for getting input from a broad range of stake holders.

Since taking over the reins of research, education and economics the mission area in USDA, Dr. Gonzalez has always strived to seek input of both internal and external stake holders. And I think everyone would agree with me on that. He's made great efforts, and he's also made great strides to assure relevance in both research, education, and extension to improve the quality

and utility of our research and education portfolio.

Without further adieu, I am delighted to introduce the Undersecretary for Research, Education and Economics, Dr. Miley Gonzalez.

[Applause.]

DR. GONZALEZ: Thank you Dr. Kennedy for those very kind remarks. I know that someone else must have written those comments that I made to the Senate, and I did mean them.

But I remember having also said to the group, to the chairman and members present, that at that point I felt like the best way to describe my learning curve was vertical. And someone said that meant going straight up, not vertical, the other direction.

It's a delight to be with you. I am very pleased to have this opportunity to thank all of you for your continuing role in making sure that we move forward with the planning and the focusing of our issues related to food safety. This conference is tremendously important. As I travel around the country, these are some of the things that as I looked at the agenda that people are talking about.

As I was leaving Phoenix the other day, I was searching around for my driver's license, couldn't find it, so I used my USDA card to show the ticket agent. And she said to me, "Are you here to check on our food, on our meat," and, she went through this long litany of things. And I said, "Yes, and I've done my job and I'm going home now."

But I do know that it is on everyone's mind. That it is important. And in the work that you're doing on the scientific and research side is tremendously, tremendously important.

As all of us that are in the room know that both President Clinton and Secretary Glickman have indicated the importance of this agenda to all of us that deal in the agricultural research and science area, but specifically as it impacts all of us, all of our citizens in this country, and certainly, when you look at the global perspective, the impact abroad.

As a part of this continuing learning curve of mine, I know that I look for the staff that we put together, the team at REE to continue to provide leadership. Eileen and I had many, many conversations, and I'm just delighted that she said yes when I asked if she would come on board as a deputy undersecretary in research, education and economics and the leadership that she's providing to our research and science agenda. And, Eileen, I thank you for that.

It's my good fortune and honor and pleasure to introduce someone to you that has been, as all of us that are dealing in this area of agriculture know, has been a tremendous advocate for and supporter of agriculture in general, more specifically, a great friend to the mission area in terms of our research and education efforts here at USDA. Those of us that have known him for some time know of his championing the effort for agriculture when he was in his home State of California, and then afterwards as he came and joined the department, and has done just a tremendous amount for all of us in agriculture, ladies and gentlemen, my good friend and boss, the Deputy Secretary, Mr. Richard Rominger. Rich?

[Applause.]

Purpose of the Conference

MR. ROMINGER: Thank you, Miley. Thanks for those kind words this morning.

As Miley said, this is a very high priority for Secretary Glickman. And many of you probably know that he is on his way this morning to Asia, or otherwise he would be here as well.

Miley, Eileen Kennedy, and their colleagues in USDA's Research, Education and Economics arm, and especially the conference chairs of Bill Wagner and Jane Robens have done a great job in putting this conference together. And they've been supported by some other dedicated and talented people from government and from academia, Lester Crawford from Georgetown University, Catherine Donnelly, the University of Vermont, Robert Livingston from the Food and Drug Administration, and from USDA, Richard Ellis and Robin Huettel, Jennifer Kuzma, and James *Lindsay*. And I want to thank all of you for getting this conference put together.

And also a word of recognition to our USDA researchers who have just moved us another step closer to safer, healthful food supply.

In the late-breaking news department, I wanted to announce that the Agriculture Research Service has developed a device that clears disease causing organisms from the air in poultry houses, protecting chicks the moment they hatch. Airborne particles, as you know, often give *Salmonella* a free ride to the chicks' feathers and lungs. And one infected chick can quickly spread the bacteria throughout an entire hatching cabinet. But this increases the risk of *Salmonella*, of course, for all of us, as adult birds are grown for food.

But using an electrostatic charge, the new device collects charged dust from the air and deposits it on the plates, automatically rinsed several times each hour. In our lab test, the tool reduced the incidence of *Salmonella* by 95 percent in week old birds and egg-laying hens. Other experiments with chicks that were already infected showed that it cut airborne transmission by 99 percent.

Well, this audience certainly isn't short on inspiration to do the job we're here for today. But this advance, I think is one more reason why the purpose of this conference, identifying the most pressing needs in food safety research is critical from farm to table.

With this national meeting, we're fulfilling the letter of the law, the Agricultural Research Extension and Education Reform Act of 1998. But I think what brings most of us here is the spirit of the law. The give and take of this conference falls in with the inclusive spirit of the legislation.

I was in the Rose Garden last June when President Clinton signed the bill. And I want to tell you that it contains 13 references to the need for the agriculture research community to get a better sense of priorities from stake holders, 13. Actually, I didn't count, but those who did, tell me that that's about right.

This conference, notably this public comment period, is, I think, a fine example of

government reaching out to bring stake holders into the decision-making process. Getting their priorities is our priority.

My thanks to the speakers who will describe the state of the art in their fields and give us some sense of where we need to go from here, and to everyone who will speak his or her mind on areas that merit more or better research.

As we open this conference, it's important that we recognize that these proceedings don't stand alone. They're part of the momentum towards safer, more nutritious food, backed for decades by publicly funded research. They're part of the recognition that the complicated mix of issues that figure into 21st Century agriculture demands research targeted to specific needs. And they're part of a bigger body of work launched by President Clinton that's already underway on food safety. The President and the public certainly have raised the bar on our food safety goals.

Let's look briefly at the whole picture, a comprehensive package of actions that are designed to protect America's families from food-borne illnesses. From farm to table, the subject and science of food safety has been elevated and are being addressed by some of the top research and regulatory minds in the Federal Government.

Starting at the beginning in America's soils, USDA is working closely with the Environmental Protection Agency on the new Food Quality Protection Act. We're working to streamline the regulation of pesticides basing decisions on the best possible science. We're working directly with farmers to implement this law and put in place new public health protections, especially for children.

Cutting across the entire food chain from farm to table, is the President's national food safety initiative. This ambitious undertaking addresses the whole continuum, advancing inspections, fruit and vegetable safety, cutting edge research, consumer education, national surveillance, detection and rapid response, and pushes our food safety efforts to a whole new level.

Recognizing that the American food supply is among the safest in the world, the initiative also recognizes that too many Americans get sick, and in some cases die, each year from food-borne pathogens. With the initiative in place, we intend to turn those numbers around.

One important development so far are new science based meat and poultry inspections are requiring tests for the first time for hidden pathogens in our food like *E.coli* and *Salmonella*. Early data show that the key to pathogen reduction, HACCP, is doing the job we set out to do.

In six months of sampling, and we caution that this is preliminary, we have documented that the percent of broiler chickens contaminated with *Salmonella* was nearly cut in half. The prevalence of Salmonella in pork also dropped significantly from earlier base line studies.

Our *Salmonella* standards for slaughter and processing plants represent the first time USDA has ever set microbial standards on such a broad scale. To bring coordination to the wide scope of the food safety initiative, the President has created a Council on Food Safety. Heading it up are Secretaries Glickman and Shalala and Neal Lane, who directs the White House

Office of Science and Technology Policy.

The council will move us, as one government, towards a seamless science based system of food safety in this country. And more important, it will put one coordinated face on the food safety mission.

I'm sure the American people probably can't tell the role of FDA versus other parts of HHS or USDA in this whole food safety issue. But I think they do know that *Salmonella* is a constant food-borne threat, and they can tell you that *E.coli* 0157 can be a killer. And they need the assurance that this council brings that their government works as one across agency lines, sharing resources and expertise for the health and well-being of their families.

Reporting to this council will be the new Joint Institute for Food Safety Research. So new, in fact, that its first public meeting is scheduled for December 1st.

The institute connects very directly to what we're doing here, because it will join the resources of the public and private sectors. It will bring together the talents of the most esteemed scientists in government, in our universities, and in business to develop cutting edge research and technology to keep our food safe. For these scientists to move strategically to advance food safety, they need to hear from you. Speaking for USDA, I can certainly say with confidence and pride that our research, education and extension system is the envy of the world. It works like a giant gear with each part thriving because it turns with the others.

Investing in food safety research is certainly one critical component, but just one. To keep pushing forward, we have to have that coordination. We need application. We need to listen. And we need to make sure that our projects step into a national food safety strategy driven by experts like yourselves.

So what we say here will make a difference. Your comments will be factored into USDA's research priorities. We're taping and transcribing all of the proceedings, as you can see. And once we've reviewed those tapes, we'll post an electronic version on the REE home page so the world can see what was said here. We'll develop a document that defines our research needs and outlines an agenda.

So I want to thank you for your hand in guiding this scientific framework and working with us. We can't produce cutting edge research in the end without direction from the best minds at the start. Thank you.

Overview of the USDA Food Safety Research Portfolio

DR. KENNEDY: Thank you, Mr. Rominger, for those thought provoking comments. I'd also like to add a personal note.

The ongoing support we get, all of us collectively in the department, makes doing our job a lot easier. So thank you.

I've been asked to make a few remarks which I think set the tone on where we want to go over the next two days.

As I look back over the past four to five years, the Clinton Administration has undertaken dramatic changes to improve food safety. Deputy Secretary Rominger has already talked about HACCP as being one of those stellar examples of success. The announcement of the President's national food safety initiative further gave advancement to improving food safety in the United States. And if you look back at the food safety initiative, of the components laid out in that initiative, two of them, research and education, relate directly to what we want to talk about over the next couple of days.

We in USDA have been working for a while, but working very specifically since earlier this year, to set forth a broad integrated research agenda on food safety. And when I say broad, it really is beyond USDA. It's a government-wide agenda.

To that end, I have had the privilege of co-chairing an inter agency working group on food safety research. My co-chairs being Dr. Bill Raub from HHS and Dr. Cliff Gabriel from the Office of Science and Technology Policy in the White House.

And a lot of our early collective efforts in thinking about this integrated food safety agenda were devoted to an assessment, first of all, of where our historical investments in research have been focused; and then secondly, and probably somewhat more important, given this historical investment and research, how do we build on these successes to focus on future sets of investments which will lead to a substantially improved food safety system in the United States.

As with the President's food safety initiative, in looking at guiding this development of a research agenda, a forward-looking agenda, we adopted a farm to table perspective in trying to define the future needs for research in laying out our conceptual framework. Put very simply, we were trying to answer the question, what should our food safety research agenda be as we move forward?

And we very quickly arrived at three overriding principles that guided us in answering this question. I have to say, first and indisputably, we agreed that the ultimate goal of where we focus our research portfolio, the ultimate goal should be to improve public health. And thus decisions about priorities for allocation of funds, allocation of staff to specific activities, will be judged in large part by the probability that this particular research, or series of research activities will lead to improved food safety, which, of course, will lead to improved public health.

Our second underlining guiding principle is that high priority has to be given to the research needs of regulatory agencies. And in particular, we want to ensure that our cadre of investments in research would ensure effective implementation of HACCP. And later on this morning, we'll hear a lot more from three regulatory agencies about the specific needs that they have.

The third guiding principle was that public sector investment must continue to emphasize preventive research. And I think the example that our deputy secretary gave this morning, again, is one classic example of how prevention can work.

Now, to make sure that the research agenda was, in fact, adhering to these three guiding

principles, improve public health via food safety, responsive to the regulatory agencies, and an emphasis on prevention, we actually fairly easily came to the consensus that the research agenda needed to be guided by a risk assessment paradigm. And this paradigm would help us define our highest priority research activities.

As we look at what has existed, what exists up until now, again, there seem to be a fairly easily arrived at consensus that a fundamental barrier to evaluating our food safety programs and our food safety policies has been imperfect knowledge about the sources of risk along this farm to table perspective. So whether you're looking at farm inputs, farm production, processing, distribution all the way to the consumer, we know that there are different risks along the chain, different risks for different kinds of pathogens.

And efforts to estimate both the benefits and costs of a whole variety of options that we have that potentially can reduce food-borne illnesses, are actually hampered by this lack of knowledge about how pathogen control efforts eventually will improve or not public health. So ensuring that our efforts to improve food safety are carefully targeted, and that we can prioritize so that we, in fact, base decisions on sound cost-effectiveness analysis is an essential goal of improving food safety, we've actually adopted this risk assessment paradigm.

Now, I know there are some people in the audience who may think that Washington types only talk to themselves. And I think to the extent that ever was the case, it probably was a mistake.

In the spirit of open and honest communication about what our priorities should be in government for investment in food safety research, we thought it was essential in crafting this research agenda and in having a forward-looking agenda that we actually get input from stake holders.

And one of the ways we did is we had an open session here in Washington on June 30th. We had about 70 organizations, many more individuals attending, talking from the point of view of both public sector and private sector investments, from the point of view of researchers involved in carrying out food safety research. We wanted to hear what they had to say.

And there were some common themes that emerged. And I'd like to, over the next couple of minutes, just limit myself to the themes that really related more to the agricultural side of the food safety research agenda.

We heard clearly, over and over again the comment that as we look at what USDA should be doing, that we need to have more attention devoted to on-farm research. Clear comment that we needed more rapid and effective methods for pathogen detection, including methods for emerging pathogens, and that's tricky, because if you don't know what the pathogen is, how does one think about techniques for detecting them.

Given what we've learned about the complexity of our food safety system, we heard a variety of comments that I would summarize as it's not simply what we decide to do as far as the food safety research, but how we decide to do it. And many individuals had very thoughtful

comments about whether or how our modus operandi might need to be somewhat different given this complexity, and that maybe we should think about more of a multi-disciplinary, multi-institutional perspective as we charge ahead with food safety research.

Again, a generalized feeling that the community of organizations and individuals involved in food safety research needs to do a better job. And I think this one is not simply for us, but everyone in this audience, what we heard was that we need to collectively do a better job of quickly sharing research, quickly sharing technology. It is a frustration that it takes a long time for that information to get out there.

Some emerging problems were clearly identified. And one that came up over and over again was the whole issue of antibiotic drug resistance. And I think, again, we'll hear about that a little bit later this morning, particularly the concern about sub-therapeutic levels of antibiotics. The feeling is that government research, at least, has under invested in this area.

Small producers may, in fact, have some unique needs. And we need to think about in our public sector agenda, how we can address some of these unique needs through research. And similar to what we've heard already, but we'll be hearing more about, a broad range of constituents said to us that there is an imperative need for science based risk assessment techniques.

So our discussions in our inter agency working group and what we have been hearing from stake holders aren't necessarily worlds apart. It's nice to see where there's overlap, where there may be some different things we're hearing.

But this collective effort of the IWG and stake holders has helped us craft a blueprint for what we see as a coordinated research agenda, coordinated being a government-wide research agenda. And I believe this will help us not only better leverage our federal dollars and our federal staff, but I think it will bring us closer to more--a more effective food safety system.

In order for this to happen, there needs to be clear priorities. And I sometimes get a little bit frustrated because I don't know what the dollar value is where I could say we have enough funds to do the job. But I don't think we're there yet.

And I think we, in government, would make a grave mistake were we to appear to be all things to all people. I think we very quickly need to decide where do we put our efforts, where do we put our funds, where do we put our other resources, and to articulate these resources based on sound plan.

By doing that, for those where you're addressing priorities on certain parts of the continuum or priorities that address certain parts of the private sector, you have happy campers. Where you have lower priorities that maybe won't be addressed until the out years, you have some unhappy campers. But, again, I speak not just for myself, but for our IWG activities, we have to prioritize in order to make quantum leaps in the utility of the research.

Some priority elements of this research agenda therefore will be, and this is my first stab at this, but it's a document which will be in the next few weeks forthcoming. And I'll give you a

flavor of what we surmise both from our internal discussions, as well as our, our--with our external partners.

Not surprisingly from the point of view of USDA, more of our emphasis will be on farm preventive research. And when I say more of our emphasis, you see this reflected in the '99 and the year 2000 budgets, and as we go forward. It's not as though suddenly a lightbulb went off when Eileen Kennedy started working on these issues.

As we have seen, if rather than taking a year-to-year perspective, if you look back over the past 10 to 15 years, we see this trend already was beginning to happen. In USDA, there's been a reallocation where once we pretty much had 50/50 post harvest, pre-harvest, resources are now both in proportionate and absolute sense devoted more to on-farm research. Research is now, over the past couple of years, already focusing more on preventive rather than therapeutic activities.

We've also expanded our agenda. Historically what we've seen is that a lot of our pathogen reduction research kind of activities have been devoted to animal commodities. We now will have a broader range of commodities that get reflected in our research agenda.

We clearly have under invested collectively in techniques to carry out the risk assessment paradigm. This is quickly changing, and again is reflected in our activities and our budgets.

In order to, we believe, in order to be able to successfully identify effective interventions, effective in part being ones that we believe employ cost effective technologies, there has to be a continued investment in basic research. And I think sometimes this message is lost.

The outside world sees the output, sees the technologies. And often, I don't think, we've done a good enough job in indicating in 1998 what it took to get to this successful product technology. And what we know is that basic research is almost always a part of that effective technology.

So in order to continue to have the technologies in the pipeline, we clearly need basic research focused that leads to a better understanding of the influence of environment. And when I say environment, I mean both the physical, as well as the biological environment, the influence of environment on pathogens, how these pathogens adapt to various stressors, and also the effects of non-pathogens present in the same environment. All of these will continue to be a focus of basic research.

Conferences such as these provide an excellent opportunity not only to share, as we will be doing, the cutting edge research that has emerged, but really to allow us in government to collectively refocus our research on potentially high payoff activities.

I listened very carefully, Mr. Rominger, to your comments this morning. And if I got it right, I think you had a statement there where you talked about the U.S. food supply being among the safest in the world. And I think you also used the term "raising the bar."

I wonder, could we not challenge ourselves collectively to raise the bar? And wouldn't it be terrific, a few years from now, to rephrase Mr. Rominger's statement and not say the U.S. food

supply is among the safest in the world, but rather, the U.S. food supply is the safest in the world.

I think we can get there. We can get there with research being a part of the solution, but also clearly very effective programs and policies geared towards better food safety in the United States.

With that, I am delighted to have the opportunity to hear from, first of all, three of our critical food safety agencies, as well as an individual who will talk about some of the technical issues related to risk assessment.

And before I begin to introduce each of the speakers, why don't we take a short 60 second break and ask each of the four speakers to join us up here at the table. And I will introduce them all at once.

And I understand that despite wanting to stay, our deputy secretary and our undersecretary, Dr. Gonzalez, must go off. But I will promise that I will, at the earliest opportunity, give you a debriefing on what happens over the next two days. And thank you for coming this morning. Thank you.

RESEARCH NEEDS OF REGULATORY AND ACTION AGENCIES

DR. KENNEDY: Good morning. Now, as people are drifting up here, I'd like to introduce our next four speakers in the order as they appear in the program. We have Dr. Robert Tauxe, who represents the Food-Borne Disease Center at the Centers for Disease Control, followed by Dr. Cathy Woteki, USDA's Undersecretary for Food Safety, followed by Dr. Stephen Sundlof, who is Director at FDA of the Center of Veterinary Medicine, followed by our last speaker, Dr. Roberta Morales, from the University of Maryland.

And what I'd like to do is have each of the presenters on the panel speak for about 15 minutes. And then that should leave us an additional 15 minutes before coffee break to have some questions and discussions with the audience.

And with that, I'd like to ask Dr. Tauxe to begin.

Research Needs - CDC

DR. TAUXE: Well, thank you very much. It's indeed a pleasure and an honor to be here this morning. And I'm delighted for the opportunity to discuss several issues with you briefly.

I'd like to start with a few remarks about the Centers for Disease Control and Prevention, my agency, and then move into some specific areas of concern and interest I think that we have identified over the past few years where a research agenda, I think, could make an enormous difference.

Let's see. Could I have the first slide, please?

Yes. We are--the CDC is an agency of the U.S. Public Health Service, a fairly young agency, actually established in World War II to control malaria in the south. At that time there was a lot of malaria in the south. And the result was that malaria was eradicated from the entire country. And that eager group that successfully eliminated that disease, decided that they would

become permanent.

And actually in 1948, our enteric reference laboratory was established. We've just celebrated our 50th anniversary. That means the branch that I'm part of, which is the outgrowth of that laboratory, is now 50 years old.

In the 1950s we adopted the emergency response mission and created the Epidemic Intelligence Service so that we're able to field epidemiologists or others as needed to assist state health departments in dealing with emergencies.

We're a non-regulatory agency. We provide independent scientific assessment to the regulatory agencies in a whole variety of different public health problems. We're epidemiologists, micro biologists, statisticians, and other public health professionals working together in teams.

Next slide, please? Is there an advance? No. Thank you very much. I guess there's not an advance mechanisms here.

Our roles in many areas of public health, including food safety, include that we conduct surveillance of public health problems, monitoring and measuring the risk to public health, and this is a variety of infectious and non-infectious problems now. We investigate new or unusual events that threaten the public health to achieve immediate disease control, but also to learn as much as we can scientifically in order to enhance long term prevention strategies.

We conduct applied research at CDC to improve the tools that are available for public health activities. And we devise and implement prevention measures, either directly for some situations, or in collaboration with regulatory agencies in industry for others. And then we use surveillance to document the efficacy of the prevention that's in place.

Now, food-borne disease in 1998 is a continuing public health concern. There are many millions of cases of food-borne disease that occur each year and many thousands of deaths.

The outbreaks that take the headlines are a small part of the problem. Actually, the great majority of reported cases are what we call sporadic, individual cases, not occurring in a setting where 100 people become ill all at once, but as individuals. This accounts for the bulk of the problem.

The challenge of food-borne disease is a changing one. There's a rapid change going on in the pathogens themselves, especially as better methods of detection are identifying more and more. There's changes in the environment. In our case, in the human ecology, they're all leading to a new array of problems.

These new problems do need new strategies for surveillance and for prevention, and open an arena for research.

Now, I view public health as a cycle, a continuing never ending cycle, with several different critical pieces to it. At the top is surveillance, the monitoring of the disease problems which identifies either a large problem or a new problem or a change in problem, which results in an epidemiologic investigation to find out more about what's going on.

As a result of that detailed scientific investigation of an issue, either direct prevention

measures may be obviously taken or a variety of new questions may be outlined that require research. And an applied research to develop those new prevention strategies leads to prevention, the third, or the fourth step in the cycle. And then, again, surveillances are a tool for measuring whether the prevention works or not.

And when prevention works, when prevention really works, diseases become rare. Typhoid fever is no longer a common problem in this country. You have to travel a long way to get it. Although if we had been having this meeting in 1898, that would have been on the top of the list for food safety. That's what successful prevention looks like.

Now, the chain of production of food from farm to table is a complex one. And I've struggled with how to sort of define it in as most a generic as possible. And I've come up with this sort of listing. If we start with the growing or the rearing of the food at the very beginning, then there are potential problems and potential issues that we have identified in outbreaks so that others have clearly identified as major issues.

The safety of the feed, the water, the manure, whether wildlife has access to the farm, and the general level of sanitation are all major issues. And resolving those issues is the right-hand side, the on-farm pathogen control measures.

Of course, as the food is produced and moves through the production chain, there are a number of other steps, all along the way, all of them having important potential points of contamination, and all of them having important potential control measures that could be in place, all the way down to the consumption of the food at the end.

I am going to focus my remarks really at the top end of this cycle, because that's where a lot of the food-borne disease problems that we grapple with start. And that's where, I think, there's the potential for some tremendous progress over the next five years.

Now, the food-borne diseases that we have identified as the most common bacterial causes of food-borne infections are a series of pathogens, most of which have very clear animal reservoirs from which they spread to the humans. For instance, Campylobacter, which is the most common bacterial cause of diarrhea in this country, pretty clearly has a major reservoir in poultry and other reservoirs, as well.

There are a variety of different Salmonella serovars which have different reservoirs depending on the serovars sometimes. And E.coli 0157:H7, which has some adaptive features that make cattle and other ruminants the primary source by which it comes to humans, and Yersinia enterocolitica, which is primarily found in swine.

Just for example, I think we are perceiving these human infections as being associated with more or less specific animal reservoirs. That means that there are some critical issues to address for these food-borne zoonotic pathogens in thinking about them and in thinking about their reservoirs. And these are sort of general research questions that I think are important to be thinking about, at least that we think about whenever we're trying to dissect out a bit more about what is happening, say, with e.coli 0157 as it's getting into various foods. These are some of the

main issues.

First of all, does the pathogen persist on the farm or is the farm just a gateway for which it passes to the food? If it persists on the farm, does it have a specific niche, a specific ecology on the farm that would offer an easy control point. And I think some may, and it's important to look for them.

What are the mechanisms of transmission that allow that pathogen to hop from one animal to another, perhaps perpetuating the infection on the farm or not? And what management practices and other factors foster or inhibit that transmission from one animal to another?

Even if the pathogen is coming in from the outside of the farm environment initially, if it persists and perpetuates itself on the farm, the farm becomes an amplification. But if there are management practices that prevent it from spreading and prevent it from persisting, then the farm environment actually becomes a barrier to food-borne disease.

And finally, I think intervention trials, once the questions up above have been answered, direct scientific intervention trials of prevention strategies are critical in a farm environment, in a model environment or in a practical farm environment to show that they work. And this could be a variety of management strategies or it could be vaccine trials or probiotics, or others. But I would, I think that the documentation that a strategy works is a critical part.

Vaccine trials, I draw the line here, because there is, for example, some interest in developing a vaccine for E.coli 0157 for children. And I have to say that I really think it's better to vaccinate the animals than the consumers, especially if we want to sell our food to anybody else in the world.

Now, to start specifically with E. coli 0157 and ruminants, it appears from a great deal of work that's now becoming summarized and available that it's quite common but transient in bovines and other ruminants. And I'm sure you'll be hearing a good deal more about this later in these, in these talks.

The specific niche on the farm is unclear, although it is clearly adapted to a somewhat acidic environment such as is found in the rumen. And it may well persist in the rumen. And we think of this as an intestinal organism, but it may be that it's really happier in the rumen than in other parts of the GI tract.

Its transmission around and among the animals in the herd is, is really not clear, although there are some important clues. One wonders about transmission through manure, although it does not appear to have a relationship to spreading manure on the pasture lands. One wonders about transmission through the drinking water, since it does survive in water. And being in the rumen means that with rumination, it would come into the cud and into the mouth, and an animal that was carrying it, could easily inoculate the water or the food that it was consuming.

The risk factors for this organism on farm need a great deal more work, and there are some, some really interesting and tantalizing possibilities. One is the constitution of the feed. And I would like to underline the problem of corn that has been highlighted in the newspapers

recently. It's not just that animals that are fed corn are more likely to have E. coli in their rumen, but there is good epidemiologic evidence that the content of the feed has a great deal to do with whether it's E. coli 0157 or not. And this becomes an immediately modifiable and immediately controllable point. And I think this is going to be a very important issue.

Rumen physiology, as it relates to E. coli 0157, needs a good deal more exploration. Why does E. coli 0157 find the rumen interesting? Does the fact that it produces a toxin have anything to do with its persistence in the rumen? There are some major questions here.

The management of the water trough looks to me like another very simple intervention point. And a good way to show whether it's a critical factor in perpetuating the organism on a farm is to manage it and see if you can stop the perpetuation of the organism. Wild ruminant access is important possibly, because it's known to be present in deer and elk and other large animals.

Let me turn to Campylobacter jejuni. Here it's very clear that there is persistence on poultry farms. It's long term. We don't know whether different subtypes are prima specific or not. That would be an interesting thing to look at, whether there's persistence that goes on through generations of birds.

The niche here is bird intestinal tract, but it's interesting and curious that deep limb tissues are contaminated somehow, because that's what people are eating. They're not eating the bird's intestinal tract. And they're usually eating something that's been cooked on the outside, but may be a little bit raw on the inside.

The questions of transmission and how Campylobacter spreads rapidly throughout a flock after introduction, could be easily studied, have been--are virtually unstudied in this country. Although there are some suggestions from European studies that water may be involved. Again, a nice intervention point.

And specific risk factors, well, if we look at a group of farms that have Campylobacter and another group of farms that don't have Campylobacter, what are management factors that differ between them? A Norwegian study of 130 flocks showed that the flocks that had Campylobacter were those that tended to lack biosecurity and that did not chlorinate their water. Whereas, the flocks that were Campylobacter free tended to be on municipal water supplies and had better biosecurity.

In British studies of one particular flock, there was persistence in the water system that was documented, a sub-therapeutic antibiotic also played a role. And cleaning up the water system and stopping the sub-therapeutic eliminated the Campylobacter from that flock. And they were able to sort of turn it on and off by manipulating these, and show that the human disease also turned on and off among people eating those chickens.

That's telling us that there may be a control measure in there, and that Campylobacter is a disease we should be thinking about as a controllable phenomenon.

Salmonella enteritidis in poultry -- this particular serotype is important. It's about a

quarter of all our human salmonellosis in the country. It's highly persistent in egg laying flocks, reappearing after simple repopulation measures. And in Europe it has also been a major problem in their broiler industry. And I think we are sort of expecting that to happen in this country sooner or later as well.

Its niches are interesting and different. It's the hen's reproductive tract, and it may also be the murine populations on farms, the mice and rats.

Here the transmission has been relatively well-defined. And it's clearly possible for it to transmit vertically. If a breeder flock were infected, it could easily pass through to the, to the next generation. But also horizontal transmission is important. The relative rule of rodent feces, the aerosols of the moisture of the manure of the litter, all seem to play a role and may need to be better worked out.

The risk factors that define management practices on farms with Salmonella enteritidis versus farms without Salmonella enteritidis have simply--have hardly begun to be studied.

And I would say this is a critical thing to do these comparative epidemiologic studies to define the importance of rodent reservoir, of the moisture level of litter, stressors, including molting, and avian infectious bursal disease, which is a common and immunosuppressive condition and may explain some of the persistence of SE in some of the flocks. I raise that as a question, one that, to my knowledge, has not been researched.

Another serotype of *Salmonella, typhimurium* DT 104 has recently emerged. This is a problem that has surged in Great Britain and Canada and the United States all about at the same time. And it now represents 10 percent of all salmonellosis and is rising.

It's an interesting strain of Salmonella in that it's quite resistant to a panel of five antibiotics, minimum. We have seen strains that are up to nine or ten now. And it very rarely causes outbreaks, though it causes a lot of sporadic illness. Those outbreaks that it does cause have been traced to Mexican style cheese made directly from raw milk, a soft cheese, and to contact with ill cattle. Both of these being bovine origin sources and the fact that there is major disease in our bovine populations caused by this same strain make it fairly clear that the bovine reservoir is important. What's not clear is whether it's the only reservoir or whether it's going to stay in bovines. It makes cattle ill, and so there has been further investigation of that.

Potential risk factors for why some farms have it and why some cattle get it is some fairly interesting practices that I would highlight as issues that need research, and perhaps change. Feeding hospital milk to calves, see, is one that has come up on farms that have had the problem. That means taking the milk from a sick animal and feeding it to a newborn calf, which sounds like a good way to spread a disease to me.

I raise the question of the safety of powder milk replacer, which calves get, and that the milk replacer itself may not in all cases be completely microbiologically safe. And I wonder if it sometimes has DT 104 in it.

And then there's the use of prophylactic or other non-therapeutic antibiotic exposures in

these farm environments. When DT 104 is there, because it's resistant, it finds that a very hospitable environment. And the more a little antibiotic gets sprinkled around to suppress its competitors, the happier it is.

I'd like to talk a little bit more about this question of controlling antimicrobial resistance and raise the concept of integrated pathogen management. Antimicrobial resistance is the result of sustained antibiotic use, which puts pressure on the organisms to select for resistance. But it's also a consequence of high levels of transmission of the organism, because if they weren't being transmitted from one animal to another, they wouldn't be there to become resistant.

So for pathogens that spread from human-to-human, the human use of antibiotics is the pressure that leads to resistance. And examples are Mycobacterium tuberculosis, gonococcus (Neisseria gonorrhea), or pneumococcus that causes pneumonia. But for zoonoses it is the use of antibiotics in animals that selects for resistant strains, such as Salmonella, Campylobacter, or E. coli.

We view prudent use and prevention strategies both as being critically needed to reduce resistance. Now, prevention means stopping the transmission on the farm or transmission from farm to table. Prudent use means reducing unnecessary uses, preserving the efficacy of those that still work, and minimizing the development of resistance in the target organisms or in other food-borne pathogens.

And I would go back to this concept of integrated pathogen management. We have to have other tools for controlling or preventing the appearance of these pathogens on farms. We can't rely on antibiotics to do the job for us.

To summarize some of these on farm management research issues as this arena for preventing food-borne disease, many food-borne pathogens have reservoirs in food animals. There's a rich spectrum of specific niches and lifestyles of those microorganisms. There's much to be learned about those risk factors for persistence and risk factors for transmission about food animals that can lead to direct prevention measures. And particular attention is needed to the role of antibiotics in developing integrated pathogen management strategies.

As an applied research agenda, I see this as a rich field that is full of new potential interventions and probiotics that could be tested, that it's critical to define practical means of reducing transmission. But ultimately I think this means bringing clean water and clean food, that is the sanitary revolution that got rid of typhoid fever in humans in this country 100 years ago, bringing that same sanitary revolution to the animal sector which really actually improve animal as well as human health.

I have to touch on a couple of other issues, because I think they're important, although they aren't sort of pathogen specific. One is the management of manure. We view manure as a potentially important means of transferring pathogens to other farms, to other species, and to produce. Pathogens survive in it. Manure is an interesting and complex substance, of course. It may have, in addition to pathogens, it may have antibiotics in it that are excreted. And there

really are no consistent standards for composting that we can confidently rely on to eliminate the pathogens of interest.

We really, I don't think, have a clear definition of what is safe. And there's a fundamental analogy with human sewage here. And I just find it hard to put it in a separate category.

Also we have a growing problem with pathogens in fruits and vegetables. We've had many recent outbreaks related to fresh produce that are contaminated usually during harvest and processing. Examples of recent outbreaks are E. coli 0157 in alfalfa sprouts, apple juice, cabbage, and lettuce; shigella in parsley and lettuce, and Salmonella on or in melons.

And this raises major concerns about the safety of the water baths, the ice that's used to chill, and compromise surface integrity of the fruits and vegetables in the field or early in processing and how pathogens can enter into the product.

And I think there's a real need for research that simulates field process and conditions to define how to prevent contamination in the first place, and to better define disinfection strategies that might be used later on.

Let me wrap up here by saying that I think that there are modifiable risk factors that can be defined for specific pathogen prevalence on farms by comparing case farms with control farms. That the growth survival and disinfection studies of food-borne pathogens in produce under production conditions is critical. Studies of manure composting to define acceptable practices are critical. And that formal trials of on farm interventions to reduce pathogen prevalence, new management changes, probiotics and hygiene are also critical.

I'd like to leave also with the thought that before we commit every last penny, to think about having flexibility for emergency research as new issues arise. Thank you very much.

Research Needs - FSIS

DR. WOTEKI: Could we have the lights up, please? I'm not going to be using slides.

I, first of all, would like to say it's a pleasure to be here with you today. I very much appreciated the invitation to participate in this meeting on food safety research priorities and challenges. And I do want to emphasize that I'm speaking on behalf of the Food Safety and Inspection Service which, as you all probably already know, is the regulatory agency within the department that has jurisdiction over meat, poultry, and egg products. So my comments are very much going to be couched from a regulator's perspective.

And from that perspective, research is not an end in itself. It's a means to an end, a way to meet a goal. And whether that goal is making sure we have an abundant food supply, whether it's a cleaner environment or safe food, from a regulator's perspective, the reason that we're--the Federal Government is sponsoring research is to help to provide the answers to meet whatever the goal is that we are trying to achieve.

So I think it's really critical that federal agencies with the responsibility for funding and conducting research establish their research agendas and set their priorities with their customers in mind. And I recognize that a regulatory agency is only one of many customers that the research

agencies have.

But clearly, setting that agenda with customers in mind is what this conference is all about today.

So for Food Safety and FSIS, I want to talk with you a bit about what's driving our agenda, talk more specifically about what our research needs are, and lastly, to pose some questions to you who are going to be participating in this conference over the next two days.

So for Food Safety and FSIS, there are really two driving forces that are at the core of both our regulatory and our research agendas. The first driving force is our goal of protecting the health of the public.

Now, in the United States, there are estimates of food-borne disease, and these estimates, although they are controversial, are the best numbers that we currently have. Up to 33 million of food-borne illness each year, up to 9,000 deaths.

And even while the Centers for Disease Control are currently working to update these estimates based on new information from their FoodNet active surveillance system, that doesn't diminish our goal or the importance of achieving that goal. And that is to reduce these numbers, whatever they are, to the fullest extent possible. They represent preventable disease. They represent preventable deaths that impose a tremendous burden on our society in medical care costs, in lost productivity, and also in personal pain and tragedy.

So to help achieve this goal of reducing food-borne disease, the Clinton Administration has deliberately and very purposefully reoriented the mission of the Food Safety and Inspection Service from a purely inspection service to a public health agency. This reorientation began in 1994 with the reorganization of the Department of Agriculture, which established the Office of the Undersecretary for Food Safety as a means of increasing the visibility of food safety within the department and separating the food safety regulatory functions from the marketing functions carried out by other parts of the department.

We continued with the reorganization of the Food Safety and Inspection Service, itself, to better prepare the agency to operate in a manner that emphasizes public health. The reorganization created a new Office of Public Health and Science with expertise that enables us to improve the scientific base needed to make good regulatory decisions that are based on public health. And we were very fortunate to be able to recruit Dr. Kay Wachsmuth to head that office.

Now, since these organizational changes were made, we can see some evidence of the impact that they've had. And first of all, the implementation of the landmark rule on pathogen reduction and hazard analysis in critical control points. Secondly, the development by FSIS of a public health driven food safety research agenda which I'm going to refer to again later in my remarks. Thirdly, the involvement, and very close involvement, with the Centers for Disease Control in the FoodNet food-borne disease surveillance system. And the fourth case in point that I bring to your attention today is the release this past summer of our first quantitative farm-to-table risk assessment for Salmonella enteritidis in eggs and egg products. It is forming the basis

of our policy development with respect to regulation of eggs and egg products.

The second driving force is a strategy, our farm-to-table strategy that Dr. Kennedy referred to already. From the very beginning of developing the food safety strategy, we've known that it must address the entire farm-to-table chain, not just what goes on within the inspected plants where we have regulatory authority.

Certainly FSIS will regulate where we have the authority, but we also feel it's very important to work through volunteering means at other points of the farm-to-table chain to encourage good agricultural practices, good manufacturing practices, and the adoption of HACCP approaches where they're appropriate.

Just as our food safety strategy has broadened to cover this farm-to-table chain, so the research strategy has to broaden to encompass all points where we can prevent food-borne disease along the farm-to-table chain.

Now, in order to achieve the goal of reducing food-borne disease through this farm-to-table strategy, we'll need a wide spectrum of resource based interventions and technologies that can be implemented on farms, on ranches, in feed lots, in food processing plants, in distribution at the retail level and in commercial kitchens and in homes.

Fortunately, we're seeing a greater focus on food safety research and more resources being devoted to this very important area, and the President's food safety initiative also has been referred to already this morning. But it's provided some new funds that have been allocated for research.

Most of this has been targeted research in a fairly narrowly defined set of priorities that are directly related to pathogen reduction, which was a major need that was identified by the regulatory agencies.

These priorities are to develop improved detection methods, to develop new prevention and intervention strategies, and to study resistance to traditional preservation techniques and to antibiotics.

In addition to requesting new funds for research, the President's food safety initiative also established an inter-agency working group convened under the auspices of the Office of Science and Technology Policy, also which Dr. Kennedy referred to. And the purpose of this group is to review the federal food safety research portfolio.

More recently, the President directed that a Joint Institute for Food Safety Research be established to develop a coordinated federal food safety research plan and program.

Now, I've made these comments because I want to make a next one to actually set the stage for the rest of my comments. And that is that the Food Safety and Inspection Service is not a research agency. We have no research capabilities, no research functions. So we have to rely on the research agencies of the department and of the Department of Health and Human Services in order to provide us with the information we need in order to perform our function.

So we also then have a responsibility to articulate what our research needs are. And the

agency has done that.

We also, very strongly support the efforts of the President's food safety initiative, the increased funding for research for food safety, the establishment of the Joint Institute for Food Safety Research, and the research portfolio review that is now underway. And we're also, we're very pleased that CSREES recently announced a new set of grants that they were awarding for food safety research and education.

Now, going back to that statement about FSIS not being a research agency, not having any research capabilities, I wanted to also point out again that we very much feel it's incumbent on us to articulate what our research needs are. And in May of 1997, FSIS published a food safety research agenda, as one means of communicating with those outside the agency about its priorities in food safety research.

This agenda is really the best articulation of our needs in support of our top regulatory priority, which is the implementation of HACCP systems in meat and poultry slaughter and processing plants.

The agenda identifies a short list of pathogens of primary concern to the agency. And it is short, there are only four of them. The entero hemorrhagic E. coli, with particular emphasis on E. coli 0157:H7, Salmonella, Campylobacter, and Listeria.

The agenda also poses a set of general questions, and for each of the high priority pathogens some very specific questions. All of these research questions relate directly to either the real time regulatory decisions that are facing the agency on a daily basis, or to longer term policy development to further enhance public health protection.

I've provided copies of this research agenda for your use during this conference. And they're on the table where you registered when you came in. So you might want to pick one up at the break or later on today. It has a rather unassuming cover. But I assure you it will be very interesting reading. And I'm very pleased with how good this really is.

But let me give you just a brief flavor, as well, of the type of questions that are raised within this document.

What's the actual incidence of food-borne illness in the United States and what's the incidence by specific pathogen and by specific food product?

What's the relationship between numbers of bacteria on raw products and food-borne illness? What are the risks along the food chain?

What's the sensitivity of sub-populations exposed to hazards in food?

How are pathogens introduced into the food chain?

Is it possible to predict emerging food-borne pathogens?

And are there vaccines or other production level interventions that would eliminate or reduce pathogens in raw products?

As FSIS conducts more quantitative risk assessment, such as the Salmonella enteritidis risk assessment that I referred to earlier, and the current one in progress on E. coli 0157:H7 in

ground beef, I think that the experience is going to help the agency to better refine this research agenda.

While risk assessments have as their primary function helping the regulatory agencies to make our public health decisions, they serve another purpose as well. They help to identify areas in which there are data gaps, where we have no information or insufficient information. Which, in turn, helps us to identify research priorities and to sharpen our articulation of those priorities.

So in closing, I believe that through the work of the President's food safety initiative, we're making some very real progress in setting a food safety research agenda that's driven by public health needs and that does have this farm-to-table focus.

However, I do have some concerns that I'd like to leave with you for your further discussion during this conference. These are areas in which I expect that the review of the research portfolio that Dr. Kennedy referred to in her opening remarks, will reveal that we've got some gaps or some very specific problems. And I think that this review is also going to need, then, to be given some very serious consideration.

There are six of these areas, and I've posed, posed these concerns as questions. And I'll go through each one of these.

The first question is, is the current investment in food safety research addressing the problems that have been identified by the regulatory agencies? In other words, are FSIS's and FDA's research agendas being adequately addressed?

In a meeting a year ago at the White House with representatives of all of the agencies sponsoring food safety research, I said that the one thing that I wanted, if I only could get one thing out of this research portfolio review, I wanted an accounting of what are the agencies doing to address the questions that we have posed in this document that had been released six months before.

And I also think that since the purpose of this meeting is to assess the research needs of a variety of audiences, I don't really think that you can fully fulfill that mission until we really have a good idea of what the base line is of support for food safety research in this country, and how adequate is it in addressing the needs of their first customers, which are the regulatory agencies.

The second question is, given the promise of on-farm interventions to reduce food-borne illnesses, does the current portfolio provide for the testing and evaluation of on-farm interventions to demonstrate their effectiveness and their costs in field settings?

I raise this question because we believe that effective interventions that can be implemented at low cost, or at least at reasonable cost to the producer, are going to be most likely to be voluntarily adopted. We have no mechanism at this time, no formal mechanism to evaluate preliminary research findings for broader testing and evaluation prior to widescale adoption although agriculture does have the infrastructure to do that.

The university based agricultural experiment station network provides an excellent infrastructure for multi-site trials to evaluate on-farm interventions to improve food safety. And

there are also some very well developed models in other areas that we could look to, to provide us with some ideas about how to set up this type of review mechanism. And I cite as examples clinical trials at NIH, the community based intervention studies that CDC funds, as well as weapons testing, the testing and evaluation the Department of Defense does. So there are other models that we can look to, to how you set up these review mechanisms.

The third set of questions are these: Is the federal investment in food safety research addressing the special needs of the small producer and the small processor as well as the large?

The food industry is really a very vibrant mix of small and large producers and processors who provide the American people with an incredibly wide and diverse spectrum of food products. The small producers and processors play a very important role in providing specialty foods, ethnic foods, organic foods, and novelties that make our lives a whole lot more pleasant and interesting. And I believe that they want to provide a safe food product. But they face some unique problems and constraints, and they don't usually have the financial ability to fund research focused on their special needs.

So I think that this qualifies as an area in which the Federal Government has a responsibility to meet their needs.

The fourth question is, is the current portfolio of research appropriately balanced as to the hazards posed by the food supply?

Our emphasis in the President's food safety initiative has been on pathogens and a relatively short list of pathogens. But naturally occurring and manmade toxicants continue to be a serious problem. Are they being adequately addressed within the current portfolio?

The fifth question is, does our current portfolio of research provide the base for our education program?

The National Advisory Committee on Meat and Poultry, which is an advisory committee to the secretary with respect to the regulatory programs of the Food Safety and Inspection Service, just recently met and recommended that more attention be paid to research on how to motivate consumers to change their food handling behaviors to improve the safety of food and to protect their families and others that they're serving within their homes.

I'd like to add that the same could be said of our education programs across the spectrum, from farm to retail. Are we funding research to motivate the behavioral changes that our research need to be made?

And lastly, is the current allocation of food safety research funds to intramural research and extramural research appropriate?

Regulatory agencies rely very heavily on the intramural laboratory system of the Agricultural Research Service. And I believe very rightfully so. Time after time, ARS has delivered research based solutions to FSIS's and also the industry's food safety problems.

But I've always been troubled that USDA's competitive grants program, the National Research Initiative, remains far below the $500 million level that was envisioned when it was

established about a decade ago. And I ask myself a question sometimes, and I know it's an unanswerable question, but the question is, would FSIS have a workable, low cost, reliable Campylobacter test now if we had had the ability through CSREES to invest maybe $10 million over a multi-year competitive grants program when Campylobacter was first identified as a leading cause of sporadic diarrheal diseases?

Now, $10 million in USDA research programs is a lot of money. That is a substantial investment. But think about it in comparison to the $1 billion a year annually that the United States pays in medical care costs for treating people with Campylobacteriosis. So a $10 million investment over a three year period of time to get us a good Campylobacter test, to my mind, is a very good investment.

But I know that that question is unanswerable. It's a "what if?" You know, what if we had done something different in the past?

I do feel that we're missing the opportunity to bring the expertise of the university community to bear on our food safety problems with our current allocation of intramural and extramural research funds in USDA.

So for the future, I think the true challenge is going to be for all of us to work together within the system that we currently have. I don't expect this conference to vastly change the allocation of research funds, but I think it would be worthwhile to think about some of these questions.

So our challenge is going to be to work together within the system that we have to try to make it the best that it possibly can be to meet our food safety goals.

I can assure you that the scientific, the public health, and the regulatory policy staff members of FSIS look forward to working with the scientific community, the food industry, and producers in the further development of the research agenda for food safety, and then meeting its challenges. Thank you all.

Research Needs - FDA

DR. SUNDLOF: Well, good morning, everyone. I'm here representing the Food and Drug Administration. And on behalf of the FDA, I want to thank all of the participants here. We're going to be relying on you heavily in the future in order to meet the demands that the public has and provide the research that is needed in order to provide a solid scientific basis for regulation and producing public policy.

Now, within the Food and Drug Administration, there are two centers that are primarily concerned about food safety. The first one is the Center for Food Safety and Applied Nutrition, and the second one is the Center for Veterinary Medicine, for which I am the director. And I want to talk a little bit about FDA's research needs and our future goals within the President's food safety initiative.

It's interesting that the public perception has really changed over the last several years. That we used to be a society that was extremely concerned primarily about chemical

contamination of the food supply. And when surveys were taken, many surveys all indicated the same thing was that the scientific community always listed microbial contamination as the top food safety risk, and the public always, always indicated that their top concern was for chemical residues, whether those were manmade or toxins or whatever.

So then with the recent outbreaks of such diseases as E. coli 0157:H7 in '97 and Cryptosporidium in Milwaukee's drinking water, the public's attention started to focus more on the microbiological contamination.

Now, it's not that the scientific community was lax in finding out or arriving at the conclusion that microbiology was where the importance should be placed, but public opinion really does drive the budgetary process. So budget for issues on food safety did not receive the attention it has up till now with the food safety initiative.

The FDA's system, we'll use science-based decisions and we'll employ risk assessments. That's how we plan to meet our regulatory goal, making food safety decisions based on science is a key part of all U.S. policy. And especially in the Food and Drug Administration, we are required by law to ensure that any kind of regulations must be based on sound scientific principle.

The President's Council on Food Safety was directed to make recommendations to the President about advancing U.S. efforts to implement a comprehensive science-based strategy to improve food safety and increase cooperation among all government agencies, both national and local. So science based policy was stressed in the President's Food Safety Council.

Also, the National Research Council earlier this year issued a report on August 20th about the U.S. food safety system and said that the food safety system must be based on science to make the best use of the limited resources available for it.

And the NRC also emphasized risk assessment. It said a comprehensive national plan should be developed that would support research and the prevention and detection of risk. But risk assessment and scientific decisions are only as good as the data supporting them. And therefore, there is a large need for continuing research.

I'll talk a little bit about some of the accomplishments that have already taken place within FDA toward the food safety initiative. But it's not just FDA. And you'll see in some of the points I'm going to be making that we could not have made the progress we had without the Centers for Disease Control and Prevention and the U.S. Department of Agriculture, because we are all working together on these issues.

Well, our research needs were listed in a document called Food Safety from Farm to Table, and that was what was issued to the President in May of 1997. It started with risk assessment. The report said risk assessment characterizes the nature and size of risk with human health associated with hazards, and to make sure the degree of scientific uncertainty of the data and the assumptions used to develop the estimates.

Risk assessments require specific information on the hazard and on the level of exposure of that hazard to the population to provide meaningful information for those making risk

management decisions. That is, for making public policy.

FDA has already joined USDA and CDC in developing one program that I'll talk about, which is the National Antimicrobial Resistance Monitoring System, which, as was started earlier, to gather more information about the actual threat to humans. And as an example of the benefit of the National Antimicrobial Resistance Monitoring Program that identified and quickly stopped an outbreak of multi-droid resistant Salmonella typhimurium DT104 that Dr. Tauxe talked about. And if it hadn't been for that system, that disease may have gone, that particular organism may not have been identified as the causative agent.

In a 1997 the FDA also formed the Joint Institute for Food Safety and Applied Nutrition. This institute allows us to capture a greater amount of research talents, because it is a partnership with the Center for Veterinary Medicine, the Center for Food Safety and Applied Nutrition, and the University of Maryland. So these are some of the accomplishments to date.

Well, what are our future research needs? And I just want to give you an overview of, now, what FDA has identified as its top priorities for research in the future. And I'll start with microbiological safety of produce.

Assessing the effect of locating animal production facilities adjacent to produce growing areas on the incidence and prevalence of food-borne pathogens on fruits and vegetables, the issue that Rob Tauxe mentioned about manure, and the effect it has not only on the water, but on the plants that are grown on soil where the manure is spread, identifying factors that can lead to the uptake and internalization of pathogens by fruits and vegetables, assessing the potential for food-borne pathogens to grow or survive on fruits and vegetables, and identifying factors, such as regional or seasonal differences, climate and damage during harvest that contribute to the level and persistence of those pathogens, assessing the potential for using quality attributes of produce as indicators of increased risk of contamination, of contamination by food-borne pathogens.

If you label certain quality aspects that would have an impact on the safety aspects. Assessing the role of insects, birds, and feral animals in the contamination of fruits and vegetables, developing quantitative models for the survival and inactivation of food-borne pathogens in manure, developing user friendly guidelines for safe use of manure, developing a means of speeding the elimination of pathogens from manure through composting, and developing a simple means for monitoring the effectiveness of that process.

Developing technologies to reduce the risk of food-borne pathogens on field packed commodities, determining factors influencing the microbiological quality of agricultural water and developing simple field methods for its assessment. Developing an inexpensive practical means for improving the microbiological quality of agricultural water, identifying non-human reservoirs for Cyclospora and the sources, factors, and agricultural practices that may contribute to the presence of Cyclospora on produce.

In the area of sprouted seeds, developing intervention technology for seed mills to reduce the incidence and prevalence of food-borne pathogens on seeds used for production of sprouts.

Assessing the effect of scarification on the potential for seeds intended to be used as sprouts.

In the area of dairy products, determining the incidence and levels of Listeria monocytogenes, Salmonella, Mycobacterium paratuberculosis, E. coli 0157:H7 and Cryptosporidium parvum in raw milk, and the identification of factors, such as seasonal and regional differences that contribute to the levels of these pathogens.

On an area that I'm particularly concerned about, and that is agricultural use of anti-microbials, there is a need for developing databases about prudent use and practices for antibiotics in food animals. The database can be used to conduct education research to determine the most effective means to educate food animal producers and veterinarians on prudent use of antibiotics.

Quantifying anti-product resistance on swine farms where specific drugs are used as part of their herd health program. The process would include tracking the animal through slaughter to determine the incidence and prevalence of antibiotic resistance in both the general microflora and pertinent food-borne pathogens on meat entering commerce.

Conducting an antimicrobial prescribing survey to determine a prescribing practice of food animal practitioner group. Production practices among cattle and swine industry and the relationship between antimicrobial use and resistance levels through on-farm sampling.

Studying the feasibility of developing and using international databases on antimicrobial resistance. This is not only an area that we have concern about from the food animal standpoint, but from the human standpoint as well. And there are efforts underway through World Health Organization and others to develop a worldwide database such that antimicrobial resistance that occurs in one part of the world can be tracked and monitored, because as we know, these microbes know no national or international boundaries. Thus, development of resistance in one area of the world can quickly affect resistance in other areas of the world.

Determining the basal antibiotic resistance patterns in cattle and determining the persistence of those patterns after clinical outbreak, including the effect of therapeutic drug treatment on pattern of resistance.

Evaluating the use of E. coli as a sentinel microorganism for predicting and monitoring changes in the antibiotic susceptibility to Salmonella. Developing a molecular diagnostic tool for detecting Campylobacter jejuni having fluoroquinoline resistance.

In the area of meat and poultry, research is needed to assess the extent to which the prohibition of feeding mammalian protein to ruminants has prevented the establishment and spread of bovine spongiform encephalopathy or BSE in the United States.

Developing and implementing molecular methodology for the protection of Clostridium perfringens in poultry production facilities to facilitate the identifying of on-farm sources of contamination.

In the area of aquaculture, there are a number of questions that need to be answered and identified. We need to identify the types and sources of bacteria, especially food-borne pathogens typically found in closed recirculating systems used in aquaculture. We need to develop models

to relate environmental conditions to the potential for unacceptable levels of Vibrio parahemolyticus and other food-borne pathogens in aquaculture fish, crustaceans and shell fish from aquatic and estuarian environment.

We need to determine the sources of food-borne pathogens in fresh water aquacultural products and identify the environmental factors and production practices that influence the incidents and prevalence of food-borne pathogens on fish as they grow and as they're harvested.

So these are some of the primary research areas. And some of them seem amazingly basic. But it's information that's desperately needed in order to form sound public policy.

Now, it is the job of the regulatory agencies, then, to translate all of this research into public policy that is protective of public health. And it can be a very difficult and complex issue. As complex as the research is, it's many times as complex to try and develop policy which incorporates that research.

Here is an example. I'll give you my example of how complex an issue it is. And that is the area of regulating animal drugs and making sure that antimicrobial resistance does not pose a human health threat.

In many ways it is a unique issue. It is different, it's a different regulatory paradigm than we've used in the past in which we've looked at the toxicologic potential of residues and made determinations prior to the approval of those products as to whether or not they're safe.

With antimicrobial resistance, it's very difficult to do. It's not possible with current technology to be able to predict in advance what will happen with in the microbial population once there is selective pressure from an antimicrobial in use. So unlike chemical residues, we can't accurately predict what's going to happen.

Resistance issues, of course, cross over to human medicine, and there is a lot of overlap between issues that we're dealing with and the issues that physicians are dealing with, for instance, with hospital-borne infections.

So we can't--we have tried, I think, in the past to force the antimicrobial resistance issue into a toxicology residue paradigm, and it just doesn't fit. So we've recognized that the old regulatory structures just are not adequate.

And the new system that we will develop, that we are developing will stress monitoring, as with the national antimicrobial resistance monitoring program, and intense surveillance. And we will include in our new regulatory scheme experts from human medicine, not just veterinary medicine, because we recognize that that is where a lot of the expertise lies.

So what is the status of antimicrobials? We think that research initiatives that we plan in CVM under the FSI, should include methods to detect food-borne pathogens in feed, we need to characterize the factors that result in multiple resistance, multiple antibiotic resistance in zoonotic pathogens. And with ARS we need to investigate methods for manipulating the microbial ecology of food animal intestinal tract and find ways to prevent colonization of animal intestinal tract with pathogen.

And working with ARS, we have approved our first product, PRE-EMPT®, which is a competitive exclusion product that is intended to minimize Salmonella colonization in poultry.

So we have a number of other issues that we must address from a regulatory standpoint. Do we have the necessary authority to take the kind of actions that we think are necessary to protect the public health?

Should we be using the same criteria for assessing the safety of therapeutic versus non-therapeutic antimicrobials?

What criteria should be used to determine if pre-approval of studies or post-approval monitoring components are needed?

Is our current definition of therapeutic versus sub-therapeutic appropriate for the current regulatory environment?

Should the establishment of withdrawal periods, the time after the drug--the time after the drug stops being used and the time that animals can go for food production? Should that incorporate issues such as antimicrobial resistance and pathogen modes?

Are there other research areas that need to be addressed?

So we have lots and lots of questions. In the years ahead we hope to find some of the answers. But we recognize that the food safety issues are complex. But by keeping it, keeping with a science base and developing risk assessment, research can yield the improvements that we need. Thank you.

Minimum Datasets for Risk Assessment

DR. MORALES: Thank you. When I was first asked to put together this presentation, I thought, oh, great, this is going to be a real challenge. And then I realized what a challenge this was really going to be, and that's because there really are no boiler plates that are applicable across all pathogens or food products for determining minimum risk assessment data needs.

What I would like to do today is sketch out some principles that may help establish what the minimum data needs are for any particular situation. And what I would like to pose to you is a couple of points for you to consider.

One is that defining the risk assessment question is the first and very key step in understanding the data needs for risk assessment. The second is establishing the pathways by which pathogens can occur and subsequently produce food-borne illness. And this is that next key step in determining minimum data needs. And Dr. Kennedy addressed this earlier as well.

And then what I'd like to do is also give you some examples based on our experience with Salmonella enteritidis risk assessment. This is work that started out as an NRI project in 1996, and ended up almost two years later as a multi-disciplinary team effort to develop a quantitative risk assessment.

What I'd like to start out by doing is first to define some terms. Risk assessment is only one of three components of risk analysis. It is most generally defined as the science of

understanding risk.

Now, risk management is a process of deciding whether or not you want to do something about that risk, and what you should do about that risk.

And risk communication is the process of explaining that threat and the related decision-making to all affected parties.

Risk assessment is the process of scientifically identifying hazards and estimating risks. It attempts to answer these questions: What can go wrong? How likely is that event to happen? And what are the consequences if it does occur?

Risk assessment aims to organize the science to provide information for policy or decision-making. Its utility lies in several areas. One is that risk assessment helps to reduce the complexity of the decision problem. It provides a means for quantifying the consequences of decision problems. It also helps, thirdly, to develop an integrated risk reduction strategy or strategies by giving information on a variety of scenarios and interventions through simulation.

Why do a risk assessment? There are really several reasons, but the most compelling of all I feel is that risk assessment lends itself very nicely to studying multi-factorial diseases or problems. And food safety is one such multi-factorial problem.

And increasingly scarce resources are compelling us to make economically sound resource allocation choices. Risk assessment provides information which allows us to compare these alternatives and to make informed decisions.

Risk assessment is a very highly organizing methodology. A large part of doing a risk assessment is organizing what you know, what you don't know, what you have assumed, and then documenting that information exclusively.

In this way, risk assessment helps to increase the transparency of the decision-making process. This is also the very same reason why risk assessment is so useful in identifying the data gaps. And those data gaps can then be used in later in prioritizing research efforts.

As I said earlier, risk assessment is a very organized methodology. And if you look at this risk assessment process, the first half of the risk really is generally what constitutes qualitative risk assessment, while the second half of the process gets into the quantitative aspects of the risk assessment.

And it's easy to see from looking at this process the importance of data to risk assessment and how integrated it is really to this process.

When it comes to determining data needs, though, for risk assessment, the most important and critical first step is to define the question that the risk assessment needs to address. And I can't emphasize enough the importance of this first step, because it really lays the groundwork for the whole risk assessment. You have to clearly define the risk assessment question that you're going to be asking or that the decision-maker is interested in so that you can then provide the appropriate information.

Because the risk assessment process is initiated by risk managers, who then they use the

output for decision-making, it is important to define the risk assessment question in close communication with the risk manager.

In defining the question, it is important to consider who is asking the question. In general, consumers are interested in knowing how am I affected by the hazard or what is my risk. So these are questions pertaining to individual risk.

The government, on the other hand, is interested in population-based risk. What are the public health impacts? And how do we decrease the occurrence of food-borne illnesses in large groups of people, or how do we reduce food-borne pathogens in animals and food products.

Industry, on the other hand, is concerned with not only their liabilities, but also their responsibilities as they relate to safe food production. And so their question frequently is, how can I effectively control the pathogen? And I might add to that, maybe even cost-effectively control the pathogen.

Now, defining the risk assessment question up front helps to establish the data needs for risk assessment. The task of identifying data needs can be focused further by addressing the question, what is the objective of the risk assessment?

Do we want to do a hazard identification? Are we interested in release or exposure assessment and those response assessment? Do we want to identify effective mitigations or interventions? Are we thinking about any specific process or are we looking at a more comprehensive quantitative risk assessment approach?

Our experience with the Salmonella enteritidis risk assessment is that a farm to table comparative assessment, which looks at the alternative motivation strategies is one of the most data intensive efforts.

Finally, determining the specific information that is needed for decision-making also helps to establish data needs. In particular, asking this last question, what information is needed for decision-making is useful for determining whether or not one needs to conduct a quantitative versus a qualitative risk assessment, and whether national or international level data is needed versus more specific data related to a pathogen, and the product processing, preparation, and consumption for its corresponding food care.

What I'd like to also now do is describe to you from our experiences in the SE risk assessment, what our data needs were, what we found that we would have been able to utilize in developing the risk assessment further and refining it.

And I think these data needs are generalizable to many pathogens in food products. In fact, Dr. Woteki earlier had listed several questions which aptly form the basis for a lot of these data needs.

The first one is risk factors. We need to be able to define what the epidemiological triangle is: a host, the agent, and environment at the farm level. Dr. Tauxe had made a reference to this earlier.

Enteritidis is probably one of the most studied of all the pathogens, and yet, we still don't

know what those risk factors are that influence it positively at the farm level.

Now, industry-specific information on various production processes are also necessary. And these are pieces of exploration that really are best gained from the industry. And these involve things such as storage and transport time and temperature.

Data on the consumer level with regard to preparation and consumption patterns, in this area, there are just huge data gaps. And this is where a lot of effort really needs to be focused on looking at what preparation and consumption patterns are, what the effects of labeling and education are on these preparation and consumption patterns.

We also need quantitative data on pathogen occurrence in food. There is a dearth of those response data, and we develop ways to obtain those response data other than the human feeding studies. Also, there is need for more information on the determinants of the probability of food-borne illness.

Pathways for each pathogens of importance need to be established. This is another critical step in the risk assessment process. We need to know which products, which processes, and which populations are involved. And this really is one of the most basic needs for risk assessment, because that's where your hazard identification comes in.

And if we want to mitigate risk, we really need data on specific interventions and their efficacy, not just experimentally, but in field situations.

To make better decisions, we really need to be linking these three approaches. However, very often we're lacking in a lot of the data, the cost data that goes into the economic analysis. And this is another area where industry can play an important role in helping to develop data.

Now, there is another reason for us to strive toward each of these approaches. That is, that there is information to be gained from each of these approaches. But furthermore, there is data that is being generated, particularly under HACCP, that should be captured and fed back into the risk assessments.

Until now all I have been talking about is focused on data and data needs and presence of data. However, the absence of data does not necessarily mean that a risk assessment cannot be conducted.

If we don't have data, then all that means is we have more uncertainty. If we have lots of data, then we're starting to move into the realm of variability of that process. What we don't know is just as important as what we do know.

In conclusion, I'd like to go over again that the data needs really are very dependent on what the risk manager's questions are. And so defining that risk assessment question is of prime importance.

But secondly, we need to be looking at the pathways for different pathogens of major importance, because this is really the starting point for risk assessment and will help establish what those minimum data needs are.

Government, academia, and industry have unique and equally important roles in the

development of data for risk assessment. While there may be exceptions, in general national level data is best developed by government since they have the resources, the national surveillance systems, the agricultural statistics in place.

However, specific data on pathogens, their epidemiology and interventions are often developed in academic settings through research. But cost, data on the cost effectiveness and field efficacy of these interventions are generally best developed by industry.

What I would like to conclude with is assert that we need to be developing partnerships for sharing data. We need to be thinking about ways of putting the mechanism and incentive for sharing data into place.

Any cooperative effort between these sectors is a step forward in leveraging the comparative advantage that each has in developing data, and is a step toward establishing minimum data sets for risk assessment. Thank you.

Dr. KENNEDY: I'd like to thank the panelists for four terrific presentations. And let me just add one comment on Dr. Morales' closing comment on partnerships.

I mean, I'd love to think about ways that we could more effectively have a sharing of data. One of the issues I didn't mention, but also comes forward as a result of our recently passed ag research bill, is the Agricultural Research Service's task with developing and maintaining a data base on food safety research. Clearly, the activities we have gone through related to the inventory of food safety research government-wide, will be part of what feeds into this database. But as we go through the next two days, I'd love to hear some discussion of how we might also use that as the nexus of actually getting the data from the private sector, and having the private sector activities be part of that. That would be one step in the direction of some partnerships in sharing data.

Why don't we take a few minutes to ask some questions before we break for coffee?

Let me start off with one.

I was taken, Dr. Tauxe, with your descriptions of how one would deal with different pathogens. But I think most of the examples you gave were ones where it was in the natural course of events, natural on-farm production activities, etcetera.

And I'm wondering, suppose we had a different scenario where it actually was a deliberate introduction of either a pathogen into the food supply or a toxin or a pathogen into the water supply, bioterrorism, what does CDC have in place that actually would allow for the speedy detection in those examples?

DR. TAUXE: Well, thank you.

I think that the basic structure of public health is like a fire department, and whether a fire is intentionally set or occurs as a result of a lightning strike, or some other natural phenomenon, may not be obvious to the fire fighters who are putting out the fire, but are determined during the investigation afterwards.

Similarly, when there's an outbreak of illness, the public health emergency response has to

be there to deal with that outbreak, to define the cause, to define what might have precipitated it and how it can be controlled in emergency fashion. And that happens with public health officials at the local level, in counties, the state, in a tiered response, more and more fire trucks can be called to the scene,and national level. I think we have emergency response systems.

The potential for a large scale bioterrorism event means we need to look very closely at those emergency response systems and make sure that they are, that they are ready to respond to something that may be at larger scale.

But when, you know, Salmonella somehow got into pasteurized milk in Chicago, and the result was 250,000 cases of illness in the next couple of weeks, that was a huge disaster. And the public health system responded to it.

I think we are an emergency response agency. Public health in general responds to emergencies. And we need to be prepared to respond to intentional emergencies as well as the thousand outbreaks that happen every year.

DR. KENNEDY: Yes, over here?

QUESTION: [Off microphone.]

I'm Jill Snowden with the Egg Nutrition Center. And I thank the speakers for their vision on these issues.

I did happen to notice an absence of comments or more specific examples on viruses and parasites. And it also makes me think that 50 percent of the food-borne disease outbreak of unknown ethology, but we don't--we may not have our schedule on causation fully identified, considering there are millions of cases of food-borne disease.

So my question is, then, is research on viruses and parasites and research and research on food-borne diseases of unknown ethology, would that be included or considered in some of your priority, and should a risk analysis be done to determine what is the risk to the consuming public if we don't take a look at some of these other micro-organisms, or even we need to identify chemical agents as well in this question, and other causes of food illness?

DR. KENNEDY: I think you're exactly right in that when we look at our historical investment in food safety research, it's been a fairly limited number of events to these limited number of pathogens.

I think one of the points that I was trying to make in my opening comments is we need to actually expand that, because there are a lot of others in which we've under invested. So in thinking about both from a risk assessment paradigm, but also more in the mode of preventive orientation of our research activities, we need to have mechanisms, research mechanisms which then feed into technologies, approaches that can be used in public policy formed by the regulatory agencies.

So there's a been a lot of discussion on that. It's not clear exactly where we'll wind up as far as our final cadre of activities, but it's a priority for our forward looking agenda.

Anybody else on the panel want to comment?

DR. WOTEKI: Well, that was actually one of my questions for the conference to consider. Do we have the right balance in the research portfolio across the hazards in the food supply?

DR. TAUXE: Perhaps I could comment, as well.

I think it's very clear that there's a lot of food-borne disease that occurs where the etiology is not defined. And I think having better tools for diagnosis available for public health purposes is a critical and unfortunately, I think, a rapidly moving area.

And that as these tools become available in state public health laboratories and other places and in clinical labs where human illness is being diagnosed or not diagnosed in the first place, I think the lights are going to go in a number of these different areas.

That's an area we haven't talked about much this morning, but that's a very actively moving forward area.

DR. KENNEDY: Other questions?

Please?

DR. HOLLINGSWORTH: Yes, Bob Hollingsworth from Michigan State University.

What I have to ask really bears on what was asked before, and that is, we seem to have suddenly lost sight of the fact that there are major chemical hazards in the food supply. The pendulum has swung, as Dr. Sundlof stated, away from a chemical hazards approach to a microbial one, and quite rightly too.

But at the same time, you can come to a meeting like this and basically hardly hear the word chemical hazard mentioned. Pathogens and food safety seem to have become almost 100 percent associated. And it concerns me. Because often other parts of Washington we've got people meeting on the Food Quality Protection Act, which is a major concern to growers over pesticide hazards. We're about to launch into spending literally hundreds of millions of dollars to test for endocrine disruptors which are mainly a food-borne hazard.

And my concern is that we're seeing a diversion here of food safety decided as microbial, and other chemical things being done completely differently by different people.

And I would like to ask whether we can bring the food safety research agenda back into a balance between the chemical and microbial hazards? It is not at the moment, in my opinion, so balanced?

DR. KENNEDY: Well, again, if I could just make a general comment.

I think this was an issue that has been and is being discussed, as we look at our portfolio, of food safety research.

I have to say in the broad range of individuals to whom we've talked, both inside government and outside, I don't sense, necessarily, a consensus on where that balance is. And, again, I think over the next two days it would be interesting to hear some discussion on where those cuts should be. Pendulums do swing back and forth.

I think the swing a few years ago in the direction of more the pathogen related research

was because the balance was skewed too much in the other direction. But where it ultimately winds up probably is going to vary by which point in time we're looking at it.

Panelist?

DR. WOTEKI: I might also add that this is a question that the President's Food Safety Council has also put as one that it needs to address.

As you know, the council has--is at the point right now where they're seeking public comment about developing a strategic plan for food safety that encompasses research as well as regulatory activities.

And among the things that we're looking for from the public and from the scientific community is guidance as to what should be the scope, the purview of the food safety activities.

Looking at how we got to the place that we are now, though, it arose because, as you know, of concern about pathogens in the food supply. The other kinds of administration initiatives that have been underway with respect particularly to pesticides have been dealt with out of a different pocket, as far as the funding goes.

So part, part of the reason was, you know, under attention in the past to pathogens in the food supply, a desire to address that got the President's food safety initiative underway. And then other mechanisms were in place and we're dealing with as other chemical types of questions.

But we do recognize that we need to bring them together, that we need to address them. And certainly among the things that we're looking for are comments about how we should go about doing that.

DR. KENNEDY: Caroline, you're going to have the last question.

Other questions after coffee, but this is the last one now.

MS. SMITH: Thank you. Caroline Smith DeWaal, Center for Science in the Public Interest. And I cannot resist asking a question of the regulators.

First, just an observation. It's interesting that FSIS, the FSIS presentation had public health as their first objective. And the FDA presentation mentioned risk assessment and sound science of their program. It either indicates a total flip flop in where the agencies have been historically or the points at which the agencies feel most insecure.

MS. SMITH: My question, my question is for Dr. Sundlof. And I'd also be interested if Dr. Tauxe had any views on it.

Several years ago you approved the use of fluoroquinoline, an antibiotic, in poultry to treat poultry flocks, which requires the antibiotic to be put into water. There was clear data from Europe showing that the use of that antibiotic resulted in the development of antibiotic resistance strains of bacteria of human concern. CDC, in addition, alerted you to the significant concern.

As a result you set up this antimicrobial resistance surveillance program, which is kind of like checking the health of the horse after they've left the barn. But, and my understanding is, data is coming out that fluoroquinoline resistant Campylobacter is, in fact, showing up.

My question to you is, now that we've disregarded science that was available from other

continents, our own sister agencies, and now that we have evidence of actual antibiotic resistance Campylobacter of human concern in this country, when are you going to withdraw the approval of that antibiotic?

DR. SUNDLOF: Well, it's a good point, and one that you've raised several times Caroline. I can tell you that the decision to withdraw any product will be based on public health issues, and that the systems that we have put in place through the National Antimicrobial Resistance Monitoring System is giving us the kind of information that will be necessary to withdraw the product if it turns out that it is a public health concern.

In making the approval decision, we based our decision on the best information that we had at the time. We had had concerns that the way the drug was being used in other countries was not the same as was being used in the United States. The fact that it's used in water is not necessarily the, the reason that bacterial resistance occurs. There are all kinds of other variables that weight into that, that process.

But, but we do have a regulatory system in place such that we can respond before there is a public health threat.

DR. KENNEDY: Thank you. I think I was right in my opening comments when I said I thought we were going to have very lively discussions. And I think this will be true.

[Coffee break.]

RESEARCH NEEDS FOR DETECTION, PREVENTION, AND RISK ASSESSMENT
SESSION II

DR. KING: We're ready to start the second session. Everybody find a seat, please.

[Pause.]

DR. KING: Good morning, ladies and gentlemen. I'm Lonnie King from the College of Veterinary Medicine, Michigan State University. The second session for the Conference on Food Safety Research is going to focus on research needs for detection, prevention, and risk assessment. We have four distinguished panelists to address these topics. Let me briefly give you their bios, and then we'll get started.

Dr. Beth Lautner will represent the food animal industries. She is a distinguished alumna of the College of Veterinary Medicine at Michigan State University, I'm glad to say. She's been in mixed animal practice in Iowa. She's had her own consulting practice. She has a Master's Degree from the University of Minnesota on research on transmission of pseudorabies virus. She's been with the National Pork Producers Council since 1991. And she's held positions of director of producer education, director of swine health and pork safety, and vice president of science and technology.

And her current position, she's responsible for food safety, swine health programs, and information as it relates to pork production and policy issues. She also helps oversee pseudorabies eradication program and disease management activities. She's active in the

American Association of Swine Practitioners, and is a recipient of the Howard Dunn Memorial Award and APHIS Administrators Award.

Dr. Richard Isaacson will talk about the ecology of food-borne pathogens in production environments. Dr. Isaacson is a native of Chicago, Illinois. His Ph.D in microbiology is from the University of Illinois. Spent four years at the National Animal Disease Center in Ames, Iowa, where he worked on diarrheal diseases of swine and cattle. Was an assistant professor in the University of Michigan Department of Epidemiology. He worked for Pfizer Corporation for six years as manager in immunology and infectious diseases focusing on antimicrobial resistance.

He is currently professor of microbiology in the Department of Veterinary Pathobiology at the College of Veterinary Medicine University of Illinois, where he is also the scientific director for the Center of Zoonoses Research and Infectious Disease.

Dr. David Nisbet will talk about management strategies and interventions for poultry and swine operations. He is a research microbiologist and project leader for swine Salmonella research at the USDA ARS food animal research lab in College Station, Texas. He's also worked as a scientist at that facility in poultry Salmonella. And that lab is now focusing on his work on human pathogens in food producing animals with a focus on developing intervention strategies that decrease colonization of human food pathogens in food producing animals.

Dr. Dale Hancock will talk about management interventions as they pertain to beef and dairy operations. Dr. Hancock is a native of Texas, a graduate with a veterinary degree Texas A&M University. Also has been a practitioner, a research associate in the Department of Veterinary Preventive Medicine at the Ohio State University where he also earned his MS and PhD degrees. He served as an assistant professor at Mississippi State the College of Veterinary Medicine. Is currently at Washington State University, where he works in field and disease investigation unit.

So Dr. Lautner, will you please get us started?

Food Animal Industry

DR. LAUTNER: Thank you. I appreciate the opportunity to present the food industry's perspective on research needs.

As I was preparing for this presentation, I actually decided to take somewhat of a different approach.

I think that important points I would like to make are that the food industry, while we recognize the importance of developing the research needs, and much effort has been directed to those, that it is really important in the future to be developing strategies to get those research needs out to the producers and where they can be actually implemented.

What I'd really like to go through very quickly here is kind of an historical review of where many of us have been in looking at research needs.

When I went to prepare for this presentation, I went to my file drawer, where I have a whole file drawer that's just titled research needs. And I went through it and looked at it and

recognized that we actually have done a lot of efforts to identify research needs. And I'd like to just quickly walk through those. So if the person's that helping me would just quickly run through those. This is somewhat historical--and I apologize for any of them that I've missed.

This was one that was done January 1993, actually an excellent summary of federal food safety research needs.

The next one that I think most of would recognize was at the time we were talking about pathogen reduction activities, there was a subcommittee report. This was an excellent report that identified many on-farm and in-plant research needs down through to the consumer.

Another important research report that was put together by FSIS preceding the one that they passed out today, was Food Safety Research: Current Activities and Future Needs. This was in 1994. This also provided very much a summary of on-farm research needs.

Another report that many of you have been involved in that Tanya Roberts helped coordinate from the Economic Research Service, that identified specifically right in the Title, Data Needs to Evaluate Control Options. This was in January of 1995.

Another presentation or group activity that many of us were involved were the technological analysis group, the TAG groups that were developed first by APHIS and then transferred to FSIS. I actually went back and re-read this report from '95. Very good research needs that were outlined in this report.

Another very good meeting that many of us attended was sponsored by the Food Safety Inspection Service, the Animal Production Food Safety Program. It was a national forum on animal production food safety. The proceedings have breakout sessions that are reported that specifically focused on research needs.

And as Dr. Woteki pointed out, in May of '97, FSIS put out a Food Safety Research Agenda, Directions for the Future that has some very specific questions, very targeted focus on on-farm research that's needed.

As we all know, the report that was out in May of 1997, A National Food Safety Initiative, Farm to Table Approach that outlined many very specific research needs. Many of us participated in the three days that reviewed what had been drafted and provided input into that process.

We also know that we have many reports out there. ARS puts out their report each year, Progress Report on Food Safety Research. This is the cover for the 1997 one. It provides a lot of input. Also identifies research needs as they talk about the impacts of that research.

So those are many of the types of governmental activities. The FDA, in May of 1998, put out a three year plan for research in support of a national food safety initiative.

And I may have missed some. If I've missed some, I haven't intended to do that. It's what was at the top of my file.

And it's not just government that's putting out a lot of reports on research needs. There's many others in industry and other groups, the Food Safety Consortium does a very good job on

identifying research needs and targeting the important priorities for research. And at their annual meeting each year, they provide an opportunity for government and industry to come forward with their research needs as well.

Also in the recent report from NRC on Ensuring Safe Food, there was some discussion of research needs and research coordination in that panel discussion as well.

Recently, I think most of you are aware of the CAST report that was a review of current recommendations that also addressed research needs. You're probably starting to see a pattern here.

And industry, we've been doing our part to contribute to the papers on research needs. The National Cattleman's Beef Association, or at that time through the National Live Stock Board, had a blue ribbon task force that did an excellent job of outlining a blueprint for industry action and specific research for E. coli 0157:H7.

That report, then, was followed up by another report that really looked at current research activity and addressed where they were from the original report to where they were at the present time.

They also had a beef safety symposium in 1997 through National Cattleman's Beef Association and the American Meat Science Association to help identify research needs and talk about priorities.

And in the pork industry, we've been doing our part to identify our research needs as well. We, each year, have special calls for proposals, do a research solicitation of what our research priorities are. And I'll just show you a few pages of what those look like.

This was our '98 one. You can go to the next one. And what we do is we target very specific research priorities. If you move that down a little, you can see. This is our pork safety pre-harvest area. And in this we identify the organisms that we're interested in working on, and specifically with Salmonella, we'll list a lot of topics under epidemiology, pathogenesis, feed, and interventions, what we feel are important research priorities and are soliciting proposals in.

This was our 1998 call for proposals. We also, have included a post harvest section in that. We have funding both available for pre-harvest and post harvest. And we'll outline what we see as important areas in the post harvest area.

In 1998 we also did a special call for proposals outside of our normal funding process to specifically call for research proposals in toxoplasmosis and antimicrobial resistance. And, for our call for proposals, we outline specifically what we're looking for as far as on-farm studies with Toxoplasma. And antimicrobial resistance we have some specific targeted areas there.

We just recently have sent out our 1999 call for proposals to the research community with those projects being due November 24th. And we'll just quickly go through. They're outlined in the same format of having a pre-harvest area that's identified.

What we do, and I'll get into this in just a minute, is we have had a Salmonella working group of scientists that sit down and each year evaluate where our research is, what the current

status is, and then say what do we need to change in our call for proposals.

And I won't go through this now, but if you will look at our 1998 call for proposals and our 1999, we actually get to a point where you can cross things off the list and say you have addressed these. We have the answer to this.

Now, most of the time, as you know, it generates the next research question. But you target, and try to keep honing down what you're trying to do in the research area. So this was the 1999 call.

And then we also have a post-harvest area as well. For this area, we have a post-harvest technical advisory group that's made of, we have some ARS scientists. We have--and I think this is a very important part, we have specific people that are responsible for quality assurance, the food microbiologists that work in the plants. And they bring forward what their research priorities are, what they see as the information that they're lacking, and what they need to know.

And this was a comment, and I think I would adapt this comment a little bit, in the Ensuring Safe Food report, it stated that research priorities and implementation strategies for common goals tend to be determined from an agency perspective, rather than as part of an integrated national program. And I'd actually, probably amend that to say from an agency and commodity group perspective we each develop our research priorities, and then have not taken those into a coordinated approach to look at the roles and responsibilities.

And I think at this conference, we're going to hear about some of the activities with the Joint Institute for Food Safety Research and the National Alliance for Food Safety that have the potential to help integrate those into an integrated food safety research agenda.

Okay, the next one.

And what I'd like to talk about is research needs, but a broader type of research needs. How are we actually going to get information out to the producer?

I was a practicing veterinarian for 12 years, and quite frankly, when I went to a farm, the producers didn't want to hear about the process that was going on, they didn't want to hear about what good work everyone was doing. They wanted the answer to the question they had for that day. And we are getting those questions on food safety from the producers. What is it I should be doing today that I'm not doing today? What is it I should be preparing for so that I will be able to do tomorrow?

Many of them are making building decisions. They're investing millions of dollars in a certain type of production system. And they're asking, what is the impact of food safety on the type of production system I'm investing in? Am I going to find out that I wish I hadn't done this?

That there are issues that may be surfacing in the research community, but that are not being expressed to producers. Do I have the information I need to make good decisions today and for the future?

One of the critical needs I think food animal industry sees is a national food safety research database, a database that has the researcher, their affiliation, what the project objectives

are, ability to sort on key words.

I know there are efforts in this, ongoing effort, but it is absolutely critical if we are going to have a focused coordinated research agenda that we have the ability to be able to look at what's being done in the public sector, across all the agencies, and in the private sector, what commodity groups are funding, what universities are funding through their own funding mechanisms, that we have access to this information.

As we all know, we don't have enough dollars to invest in duplicative research. We need to know that we've got the scientists connected that are working on an issue.

I'm still surprised sometimes when we're looking at a specific issue and putting together a working group on it, that we've missed somebody that's working on that area, because we just didn't recognize that they were in that field. They were maybe at a less well known university, hadn't been at some of the meetings, or maybe off by themselves doing the research, but providing a very critical piece of information.

I think this research database, and I'm sure there will be discussions on this, is absolutely critical as we move forward.

And as I said, a national food safety research agenda that's an integrated research agenda, that allows you to look at what's being done and be able to set benchmarks for progress and to know that you're on the pathway to solving problems with information.

The next overhead.

A couple of suggestions on how to do some of these types of things would be that to form collaborative species-specific, pathogen-specific working groups. I think if I ask how many really bench researchers were in the room today, I think it would be a very small number who are actually involved in research on the day-to-day basis in the laboratories.

And I think it's very important that we get the people together that are working on the issues to specifically look at that issue, identify research needs. It is a way that you can communicate information prior to the publication, those types of things. People can give indications of areas that they're looking at. You can identify collaborative research projects.

One of the things that's happened from the working groups we've developed on certain topics is that when you get the scientists in the room, someone says, well, I'm interested in looking at this aspect. Another scientist said, well, if you'd
send me those samples, I would look at this, because this is my area of expertise. And you allow the ability to have better collaborative projects.

As Dr. Woteki said, I think I can't stress enough the importance of on-farm demonstration projects. We cannot go to the field to producers and say you have to change what you're doing when we've got laboratory experiments based on two animals. It just can't be done. None of us are going to go out there and try to convince producers to do something that we don't have field experience with. We need producers themselves that have implemented some of these intervention strategies that can stand up and talk to their peers and say, hey, here's how you can

integrate it into your daily operation. It's possible to do this.

And we absolutely need those types of demonstration projects, because I think, as we all know, what works in the laboratory, when we get out into the complex setting on the farms, we have many other factors that may not have been able to be accounted for in the laboratory.

And I'm going to stress again and again the value of technology transfer. And we've been very guilty of this, I think, at our organization. We feel real good when we publish a research report that's about this thick. Summarizes all the research we've funded.

I don't think I've found a person yet that's read it. And I think it's very important that we start taking that information and breaking it down and getting it targeted to the audiences that need to know it. I've got a couple comments on that in a minute.

An evaluation process, we need to somehow have a way to evaluate the progress we're making in research. And I put risk assessments in there, because I know we have to say that all the time. And I think that is important, I'm not trying to be facetious, but it is important, we have to go back and look at the pathway we're going down in this research area, is it going to contribute, is it important to the overall scheme? Is it going to provide information that we need for risk assessments?

Okay. Next.

Now, quickly, I'll just run through some ideas of different things that different groups have worked on.

The National Pork Producers Council, we have developed specific working groups. We have a kind of working group, we're doing an on-farm herd certification program that will be launched next year. We have a toxoplasma working group looking at what we can do on the interventions at the farm level. As I said a Salmonella working group that gets together, identifies where we're at in the research; where we need to go. A post harvest food safety technical advisory group made up of university researchers, government researchers, and I think most importantly, the industry that brings their questions that they need to resolve.

We have a packer processor industry council that we go to and ask them specifically what kinds of things do you see ahead. We have a retail action force that's very interested in food safety. That we have done some retail studies that we have conveyed to them, and they've helped design those projects.

These are--we also are working internationally with two other countries to look at food safety systems internationally. What is it, the types of things we need to be doing on-farm, what do we need to be doing in the plant. And all this feeds into our pork safety committee that's made up of producers and academia and people from the industry.

Some examples of activities that have been ongoing and a way to look at research, this is done by the beef industry, looking at the status of current research. And I just wanted to show these matrixes as an example of a way we, perhaps, could try to summarize information in the future.

You're not going to be able to read this, but this is a pre-harvest food safety matrix. And across the top they have different targeted areas, like host-pathogen relationships, factors outside the host, incidence, sampling methods.

And what they've done is identified what research projects go under those main category headings. And then to look at how are we doing in that area, they actually color code the areas. The green means we've got projects in that area that have been completed and published. The yellow means we've got ongoing projects of these titles in this area. The red means we don't have funding to do these types of activities. This is a very graphic presentation to help you understand where you are in research agenda.

I'll just show one more of those. I think I've got several of those, but I'll show one more.

They also have developed those specifically when they look at E. coli for carcass conversion, they've looked at it in the plant. And I'll just skip through those.

They also have those for food service and other parts of the chain and consumer food service. And then we'll go to the next one.

They have one also, I think, identified for consumers. But it's a nice way to graphically present that you have a research agenda, that you have progress ongoing, and you can identify areas where you need to take a look at it.

So I think that's one format that we may want to take a look at in the future.

As far as technology transfer, one of the things we've done is created a publication called Tech Talk that we send out to people in the industry that gives short synopsis of research, very quick, new research that's just come out. And we provide this out to the industry and also provide a contact if they want more information on that specific project. This one was on developing strategies to prevent salmonellosis. And there's a lot of other technology transfer type of activities that can take place.

All the commodity groups have quality assurance programs to deliver information, or transfer the technology to producers. These are ways that we've already established that we can put information in and transfer to producers.

I'll just show a couple more types of technology transfer activities.

We try to explain to producers what HACCP is and put a video out to explain what HACCP is and what the implications are for producers of HACCP. So there's a variety of educational tools to use to transfer information.

We're also working on one for rodent control right now for producers; how it will take specific types of buildings and show you how to implement rodent control.

There have been several meetings on specific topics. This has been a very good USDA, FDA, MPPC, and the feed industry effort. We started in '96, the first international symposium on Salmonella in pork production. And we entitled it, the first one, with not knowing whether there would be anymore to follow, but this has been very successful. This was internationally attended. Denmark then came and picked up the next one, had the last one in August of '97.

And I'd like to just show that the next one on Salmonella in pork production will be held in Washington, D.C. August 5th through 8th. And I think this will be an excellent opportunity. It covers Salmonella control across the chain. It will be an excellent opportunity to get up-to-date on international research in this area.

I will put some brochures out on the table if people are interested in attending this.

We also held a quality safety summit for technology transfer in July where really cutting edge information was delivered and which was attended by people from the plants and practitioners and producers.

And I think I'd like to just summarize that I think what we're doing today is very important. What has been done in the past on identifying research needs is very important. We need to have all get on the same page with regard to research needs.

But I think it's critically important that we take the next step, that we get a coordinated research agenda. And in that research agenda, we include how we are going to deliver the technology and transfer this technology out to the people that can actually use this and are actually anxiously awaiting this type of information. Thank you.

Ecology of Food-Borne Pathogens in Production Environment

DR. ISAACSON: Could I get the slides on?

Well, I want to thank the organizers of this meeting for allowing me to speak to you today, giving me the opportunity.

I was charged with discussing the microbial ecology of food-borne pathogens on-farm and trying to describe where we are and where we should go. And I think probably the answer to that is, where should we go, because there's not really a whole lot to say about where we are to date, because we're really beginning.

And a lot of what I'm going to have to say is going to be somewhat repetitious of what we've already heard this morning. But I hope to be able to take a bit of a different tact on it, as well as taking more of the organisms viewpoint and trying to show you some data occasionally to demonstrate where some of the problems are.

Now, the underlining guidelines of what I want to say and where I think we need to go is based on the National Academy of Sciences statement that what we really need to do is base any decisions on science. And so what I'm going to try to tell you about is where I think there are needs for investigations that will lead to understanding the science of microbial organisms on-farm, and specifically the food-borne pathogens.

In the next two slides I want to give you the punch line up front, and then go back and talk about the different areas that I think need to be worked on.

I have divided up the areas of importance into two areas, one of which I'm going to call HACCP based, which is focused on trying to identify critical control points which can be used to

develop passive principles on-farm. And these things in my mind include topics such as the source of the microbes on-farm, the distribution and prevalence of those organisms on-farm, how those microbes are transmitted back and forth amongst animals, and other reservoirs on-farm within the herd.

And then a discussion of a phenomena that seems to be common to most if not all of the food-borne pathogens, and that is mechanisms of persistence, how they maintain themselves on-farm, in what would be otherwise clinically healthy animals.

What are the production practices? And this really leads to identification of risk factors that lead to the presence of pathogens. And then an area which is sort of common to all livestock production which deals with the issue of transportation at the end of the production cycle to the slaughter plant and the effects of feed withdrawal on that process and on the shedding of organisms as they enter the slaughter plant.

You could argue that some of these are not necessarily HACCP based. I put this group into a non HACCP based area. And I'll talk a little bit less about these. But there is really a critical need within the research area, as well as the intervention area, to have better pathogen detection techniques. And I'll talk a bit about that from two aspects.

We need to then evaluate all these data in terms of risk assessment. And as a microbiologist, risk assessment to me is something very mysterious and difficult to perform. But fortunately there are people who do that.

I also want to talk a bit about resistance to antibiotics, and the impact that has on the population. And then ultimately that has to be converted to a discussion of the economics of this risk--the cost of risk benefits.

Now, before I actually go in and talk about each one of these separately, I put together what is my list of important microbial pathogens. These are in a somewhat prioritized level to me. And that means that we put at the top of the list, or at least at the top of my list is Salmonella enterica (multiple servars0, and Campylobacter jejuni, which is probably, at least in terms--probably of equal importance. The emerging pathogen E. coli 0157:H7, and one that's starting to be more recognized, Yersinia enterocolitica, and Listeria monocytogenes. And they do have two non-bacterial organisms that are up here that are also in consideration in the food safety portfolio.

I haven't put any viruses up there, because at this particular point I don't know that we really know whether at least from the on-farm standpoint, whether viruses are important in getting into the food chain at that level.

However, there have been some studies that are beginning to be done, particularly by Linda Saif at Ohio State, that are starting to question whether or not there are viruses in animal populations that are getting into the food chain and are causing food-borne illnesses.

Now, let me just also tell you that most of the way I'm going to try to discuss these separate issues is going to be based on my understanding of what's out there. And I will talk primarily about swine systems, because that's what we work in. And I will also talk primarily, but

not exclusively, about Salmonella, because that's also what we worked with.

But I would also argue that what we learn from Salmonella can be applied to other systems and what we learn in swine can be applied to other systems. But we have to be aware that there will still be differences. And I'll point some of that out when we get into persistence.

So the first areas that are, to me, important are the sources of the microbes, the distribution prevalence, and the transmission.

We've been involved in a number of studies at Illinois looking at the sources of microbes and also trying to identify transmission patterns, risk factors. And we aren't the only ones who are doodling in this area. There are numerous laboratories who are focused in on this, this particular kind of a target.

What I want to show you, though, is what's kind of an interesting outcome, is that in the analysis that we've done so far, which is really based on six farms where we knew that Salmonella was present, is that we have looked at a number of different reservoirs or sources that might be reservoirs for Salmonella. And what I can tell you is literally every place that we've looked, we've found Salmonella.

Clearly, we found it in young pigs, maturing pigs. We found it in sows. And my bias is that, that these are probably the major reservoir for transmission on-farm.

But we've looked in water, feed, booths, floors, we've collected a number of insects, we've also collected rodents and cats that are on the farm, and literally every type of sample that we have collected, we have found some level of Salmonella present on-farm.

So the point being is that when it's there, it's probably there ubiquitously. It's probably present in all sorts of different sources. And part of the question will be ferreting out whether any of these are relevant to the transmission of these pathogens to the animals or whether or not they're simply a consequence of their being in an environment where these animals already live.

Let me talk about distribution and prevalence. Again, using the swine model in Salmonella, we've looked at slaughter plant samples from about 150 herds in Illinois and asked for the presence of Salmonella in both the herds and in the animals. And we're coming up with a value which is now emerging as a common figure. We find that probably 60 percent of all the herds that we've looked at so far are carrying Salmonella. And I'll tell you, that's a minimum estimate, because the methods that are used are grossly inaccurate in my estimation.

And when we look at the animal specific prevalence, we're looking at somewhere between 18 and 20 percent.

So going back to what I was saying before, this is an organism that is pretty ubiquitous in nature. It is out there. In fact, we're moving to a point, at least I'm moving to a point where I'm starting to think of Salmonella, which always to me was a pathogen, as being something that is, that might be considered in livestock animals as normal flora.

And all of the animals that we've sampled were selected as being healthy. These are not ill animals. So in the healthy population, we have a very high prevalence of these organisms.

Now, I thnik that we're starting to get a fairly good handle on issues of distribution and prevalence.

The real question is the transmission, because if we really want to get involved in HACCP-based intervention, then we need to know where the patterns are that can be blocked to get transmission into the animals.

And this is an area that, that we're trying to get into ourselves. I don't think we have any good answers at the moment, but the point would be is that when you look at sources like this, when it's everywhere, you have to really debate which are the relevant targets for blocking transmission into animals. Is it, for example, in water simply because the water is contaminated initially or is it the animals who contaminate it themselves?

Are the insects carrying it and spreading it from pen to pen, or is it that the animals are already shedding it and the insects moving from pen to pen happen to pick it up? So there's really fundamental work that, that needs to be done to answer this question.

Now, one of the really key things that we've been dealing with, and one that I think has been neglected in the past, is dealing with the question of on-farm persistence of microbes.

When we look at food-borne pathogens in general, there's a lot of work done on the pathogenesis, particularly in human and in that human model called the mouse.

There's very little work, actually,in livestock animals, looking at how it can maintain itself.

There was a, what I thought was a fundamental study done back--and published in 1989 by Dick Wood, who was at NADC at the time, in which he took a group of pigs, and he challenged them orally with Salmonella typhimurium, and then followed them over time to see whether or not they were still shedding Salmonella. And after an initial--shortly after the challenge period, these animals recovered from a brief, transient illness, but the rest of the time, these animals remained healthy.

And the point of this is that at 24 weeks post-challenge, when these animals achieved market weight, they were still colonized with Salmonella typhimurium.

We've replicated this experiment using lower challenge doses, and we find a very similar thing, except that occasionally--or, in fact, usually at the end of this time period, it goes off to nothing. But that's very misleading. So there is this mechanism involved, that Salmonella, and probably other microbes, utilized to maintain themselves.

This slide is sort of my mechanistic slide, and I'm not going to go through it. It's here to tell you that we have specific hypotheses about how, in this case, Salmonella can persist in animal populations for long periods, and we think that there's a unique genetic switching mechanism which allows Salmonella to switch back and forth between two phenotypes so it can maintain itself at a very low but constant level in animals, which will cause what we would then say are sub-clinical infections that are asymptomatic.

Now, what's important to note here is that this is a model that we've put together for Salmonella. Salmonella is inherently invasive. When it comes into contact with any kind of

eukaryotic cell, it enters. That's the nature of Salmonella.

E. Coli 0157 doesn't do that. E. coli 0157 is a mucosal pathogen; it does not generally invade. Campylobacter jejuni also is primarily a mucosal pathogen, although there is evidence that it will get into eukaryotic cells, and it can survive, as well, in eukaryotic cells in a way similar to Salmonella.

The point being is that in this case, while there are probably common themes of persistence or, possibly, continual re-inoculation, that the mechanisms are clearly going to be different, and we need to identify what they are going to be.

And perhaps this is maybe a bit out of order--people have been now looking--and we're involved in this, looking at risk factors. We've heard about risk factors today already several times. I will also plug the fact that we need to identify on-farm production practices that lead to the encouragement of certain pathogens being on-farm.

But I think we need to take it and--no one has quite said it this way, so I will make sure that we are on a common theme here, or a common plane--that when factors are identified that statistically look as though they may be involved in allowing a specific pathogen to be present on-farm, that we then have to go in and try interventions to see whether or not that's really true.

And this is really a bit of a problem, because--if you recall with the Salmonella issue, that there are so many potential reservoirs, that intervention by blocking transmission from one reservoir into the curd may simply have a negligible effect, and that there will be multiple sites.

So it's likely that an identification of risk factors, and trying to develop passive programs, are going to be more than just single targets. I suspect it's going to involve many targets.

Now in the HACCP area, the last one I want to talk about is transportation stress and feed withdrawal.

All animals, except some unique ones that are going to slaughter, are transported. And we, and others, have published descriptions of the fact that when they're transported they undergo a stress response, and that can increase the shedding rate in feces of specific pathogens. Also, feed withdrawal is a fairly common practice in the livestock industry. And we also know that that practice has some effects. And I just want to show you some of the data that we've obtained recently regarding transportation stress and feed withdrawal.

In this particular experiment we challenged some pigs right after they were weaned. We then reared them conventionally until they hit market weight. And then we subjected them to transportation stress. They were all transported for about 150 miles. They were also divided into groups that had different levels of feed withdrawal. And when we combined feed withdrawal with the transportation stress, you can see that there's a direct correlation, in this particular experiment, between feed withdrawal--so over the longer time of feed withdrawal we see a greater number of shedding animals in the population.

Now, the ones that remained on feed in this particular experiment had the lowest level of shedding. That isn't always the case. Sometimes we see it the other way around. And I should tell you that this is also above baseline. In fact, all of the animals that we looked at, with the exception of about three at this time--in this group of 48 animals--were designated non-Salmonella-containing animals by analysis prior to feed withdrawal and shipping.

And the mechanisms involved in this are really important, because of the fact that these stresses are going to be ubiquitous to most livestock animals going to slaughter. And therefore, if we can understand the process of how transportation stress and feed withdrawal induce this increased shedding, there's the potential to then develop strategies to intervene.

We've had a program--or project, in fact, that this started out as. We called it the "Piggie Prozac Project" --

And so if we can make them happy before they go, perhaps that will reduce the shedding rate.

Okay. Pathogen detection. It's pretty clear that if we're going to do anything on-farm--particularly if you want to be able to identify animals that are positive and negative for any particular pathogen, we have to have techniques to do this--both on-farm and in the slaughter plant. These have to be rapid tests. We're in time constraints. They have to be sensitive, and they have to be amenable to operation in more field-like situations than the specific laboratory situation.

Secondly, pathogen detection also falls into a second category. So we need sensitive methods, but as I mentioned a moment ago with our transportation stress studies, not all the time do animals that we know are carriers actually show up as carriers. And just to give you an idea of this, in that transportation stress study, we followed the shedding of Salmonella in feces over time, and you can see that initially we had a very high shedding rate, in fact even though we never achieved 100 percent at any one time, 100 percent of the pigs that we challenged were positive for Salmonella at some sampling time.

But at the time just prior to their going--being transported, it was only a couple percent that were actually positive. I think it was actually three pigs out of 48 that were positive. But once we transported them, particularly in the most highly stressed group, we found that over 80 percent were positive.

And so there's a question of: how do you detect the pigs that are in this group here, that aren't shown by any bar. Those are the group of pigs that are potentially a source of contamination in the slaughter plant, and yet there's no way of predicting, *a priori*, which one's they're going to be.

And that leads to a question of how are we going to do this and, more particularly--if anyone wants to have a Salmonella certification project--or program--how in the world are you

going to certify Salmonella-free animals without being able to, with any certainty, know whether you have positive animals.

So there's an important area that needs to be looked at here.

The last couple of areas that I want to talk about very briefly is risk assessment. We find that in all of the samples that we collect at the end of a challenged period, which is when they hit market weight, that the concentration of organism is very low: about 100 microbes--roughly, in the case of Salmonella--per gram of feces, which is a pretty low load. In fact, it's probably below the infectious dose for humans.

What risk does that pose? We don't know. And what risks are downstream that allow that low dose to be amplified? We need to understand that.

We've heard about antibiotic resistance. Antibiotics are used ubiquitously in livestock production, both for therapeutic and growth-promotion purposes. We're pretty sure that the use of antibiotics on-farm leads to antibiotic resistance, particularly in zoonotic pathogens, which is probably a fairly straightforward concept, but we need to, in fact, establish that that's true.

But more so, I think there are two other questions that need to be addressed in this, and that is what is the impact of antibiotic usage and antibiotic resistance in non-pathogen populations, in terms of transmission to other human pathogens?

And, secondly, as a corollary to that, what is the contribution, then, of those non-pathogenic resistance genes--that is, coming from the non-pathogens--in contributing to pathogens that you would not find normally coming from animals, such as Enterococcus, Staphylococcus, Staph aureus--those types of organisms--does this reservoir pose a risk to create resistant organisms that one might find in the hospital? And I think those are important questions, because agriculture has been--had a number of people pointing at it, in terms of its antibiotic usage, in terms of the impact that it's had on human--resistance in human pathogens. And I think we need to establish, one way or another, what the case is.

And then, finally, the obvious is--tied with the risk assessment, is what is the cost of all of this and what kinds of benefits do we get for these costs; and making assessments as to, then, what are the most appropriate ways to go.

In the end, I think that what we're going to need are several tactics in order to control microbes. We're going to need answers to all of these questions. And, ultimately, I think that if we can answer these questions it's going to be possible to effectively begin to use on-farm HACCP programs.

And, with that, I'll stop. Thank you.

Management Interventions:
I. Poultry and Swine

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DR. NISBET: As Dr. King previously mentioned, my name is David Nisbet, and I'm from the USDA-ARS in College Station, Texas. I represent a fairly large laboratory that does a lot of diverse types of research. Some of the research projects that we're doing in our laboratory have to do with intervention strategies, and the intervention strategies that we work with in College Station have been competitive exclusion--and I'll talk about that today. We also do gastrointestinal modeling as a consequence of what we've learned from our competitive exclusion research. We're also a laboratory that develops rapid immunological assays. And, over the last six or seven years, as a result of our competitive exclusion work, we've been able to do an awful lot of field trials with both--mostly with poultry, but some with swine, around the country. And from that type of research we've learned an awful lot about where we think we need to go, and what type of technologies that need to be developed, and the technologies that we have today on the market, where they actually fail, and how we can address those issues.

First, I'll just tell you what competitive exclusion is. It's the prevention of enteropathogen colonization by normal intestinal flora in poultry, and it's really a very simple concept. All you do is you take normal flora from an adult bird, or an adult pig, and you give it to a young animal, and it confers some sort of resistance against pathogen colonization on that young animal. And, in some instances, within the production system it can be very effective.

And this is just a slide showing you some field data that we've accumulated. This is from an FDA experiment for the approval of a product that we've gotten on the market through our laboratory. Control chickens had a 7.2 percent colonization rate by Salmonella at the end of grow-out, and when they were given a product developed by the USDA, we call this product "Preempt" now, those chickens were actually protected against Salmonella.

And so these products can indeed work. They can be a very good intervention strategy, but they do have limitations, and those limitations have made us look at what else do we have to do to support this technology.

One of the problems that we have with competitive exclusion: it is, indeed, simply a prophylactic type of intervention strategy. If you already have a flock of chickens that are infected with something like Salmonella, then don't use a competitive exclusion culture. It will not work. It's not the way the technology works.

One of the problems that we have with competitive exclusion at the end of grow-out, we have feed withdrawal. And during the grow-out period, animals are defecating and putting Salmonella into the environment. When we withdraw the feed away from chickens, these chickens are programmed to do simply one thing; they peck at the ground. And when they peck at the ground, they re-inoculate themselves with Salmonella. So now, again, you have a bird that's re-contaminated just prior to going to the processing plant.

So, although we have shown that competitive exclusion cultures can reduce the level of

pathogens in the litter of chickens where they're raised, there's still some there, and so they can be re-inoculated. We need to develop something to address that particular issue.

What about these guys? Most recently, because of the success we had with our poultry product, we've been asked to develop the same type of technology for the swine industry, and to see if it will actually work.

Within the swine production system, we see intervention strategies such as competitive exclusion or other types of microbial intervention strategies best used, probably in two different spots: baby pigs--baby pigs are born with an open, or a naive gastrointestinal system. We know that these very naive gastrointestinal systems are highly susceptible to colonization by pathogens. We need to do something to speed up the maturation of these baby pigs' guts so that they have some sort of resistance against pathogens.

And then, once again, just two weeks later, or even less some days in industry, we wean these pigs. When you wean pigs, you change their diet. When you change a pig's diet, the microflora which is in the gut of that animal can change dramatically. It's dependent on the diet that that animal's on. Any time a pathogen such as Salmonella, which is an opportunist, sees an opportunity like a disordered gastrointestinal system because of change in diet, here comes Salmonella again. That's where it likes to live. That's where it's going to go. So we need to develop things during the weaning process of these animals that can give them some resistance during these times.

One thing we've found is horizontal transmission of Salmonella within the swine population is very important, even in very young animals. We had originally thought that there wasn't much Salmonella in baby pigs, and things like Salmonella--or serotypes like Salmonella cholerasuis--begin to appear after the weaning process. Well, we always wondered where did it come from? Salmonella cholerasuis is a host-adapted pathogen. It's not likely in the rats and in the environment. It's coming from someplace and we thought, well, the baby pigs may be getting it from their mother, and then it's being expanded throughout the growth of those animals.

So we've done several experiments with an integrated producer in Texas, and we've shown that animals from their swine facility at somewhere between 9 and 14 days of age generally have somewhere between 7 and 10 percent of those animals are positive for Salmonella. We take those animals and co-mingle them together in a fairly clean environment--these are experimental conditions, where we actually clean up everyday. We see an amplification of Salmonella within 48 hours, approximately sixfold. We go from 10 percent of those animals positive, to 60 percent of those animals positive. So we have to design a strategy, during the weaning process, when we co-mingle these animals to sort of interfere with the spread of Salmonella during that time.

Competitive exclusion is somewhat efficacious at doing this. We've done experiments where we've measured the horizontal transmission of Salmonella in animals that have either been

treated with a competitive exclusion culture or not treated. We see our animals--almost all of our animals that don't get the CE culture shed at some time or another. The shedding incidence of those animals is a cumulative number--52 percent. When we give a competitive exclusion culture prophylactically, we can reduce that somewhat over 50, 60 percent. So CE can actually work in this process also to decrease horizontal transmission of Salmonella during weaning.

This is just a graph showing this kind of data from several experiments we've done. Here's the incidence of shedding of pigs between 14 and 21 days of age which have not been given a competitive exclusion culture. We see somewhere around 80 percent of those pigs, as a cumulative number, have been shedding Salmonella at one time or another, and we see that reduced across our experiments down to somewhere around 20 percent when we use this as an intervention strategy.

So, competitive exclusion does have some merit, possibly, for use in the swine industry. It's certainly not a cure-all, but it's just an example of an on-farm intervention strategy.

So, I guess, competitive exclusion, from our laboratory's perspective--what we've learned during the past six or seven years--is where do we need to go from here? What have we learned from field trials we've done, the products that we've developed? Where do we think we need to address issues for on-farm intervention strategies?

Well, when it comes to competitive exclusion, one of the biggest problems with it is: what are the interactions with antimicrobials; with antibiotics that we use today? We know that if you use antibiotics in your starter feed in chicks, that that can have a real profound effect--a negative effect--on the efficacy of a competitive exclusion culture. It--competitive exclusion--is indeed a microbial intervention strategy, so the antimicrobials that we use can kill the product, rendering the produce somewhat useless. So what is that actual effect on efficacy? What antibiotics are compatible, and which antibiotics are not compatible with this particular type of an intervention strategy?

And also another issue that I think really needs to be addressed is: what is the antimicrobial resistance patterns of the competitive exclusion organisms themselves? If competitive exclusion gets adapted and used in the industry--we have 8 billion chickens that go through this country a year--we don't want to be giving them cultures of bacteria that we don't know what the antimicrobial resistance patterns are of those cultures. So that's very important data.

And we actually have that data. It was one of the things that the FDA asked for. So it's very important and that we monitor these things.

It's very difficult to find out about antimicrobial interactions with normal flora, etcetera, and do this work in animals. A couple of reasons: chickens, it's fairly inexpensive to work with, but if we want to work with pigs and do this type of research, it's extremely expensive. So what

we--at least in my mind. what we need to be able to do, is we need to be able to model the gastrointestinal tract so that we can make decisions, and understand what's going on inside that system.

We need to increase the information that we have on interactions between gastrointestinal tract normal flora and enteropathogens such as Salmonella. Currently, we really don't know very much about the physiology of what's going on in the gastrointestinal tract and how these organisms are interacting with each other.

We need to be able to use models of the GI tract for risk assessment for the use--or the non-use--of antimicrobials in agriculture, and we need to be able to use models to find out what are the events for acquisition of antimicrobial resistance by pathogens.

We need to use models to find out what is the impact of antimicrobials on the normal flora, and how does it decrease the normal flora's ability to defend against Salmonella colonization in the GI tract of an animal.

We also need to be able to use models to develop better microbial intervention strategies. And it's a lot cheaper to do this with models than it is to do with animals, particularly when we're talking about swine or bovine. We did research with chickens for six years. It cost me 35 cents to buy a chicken. It cost me $35 to buy a pig. We do research--we may buy five sows. Sometimes we'll get one baby pig from that sow, and she cost me $500, that becomes very, very expensive, and you can't really solve--or answer some of these questions on the budget that we have for that. So I think it's important that we develop some sort of risk assessment models.

There is another reason I think models are very important--and this has always griped me, as a microbiologist--kind of a background in microbial ecology. When you get information on Salmonella, basically most of the information that's published is based on Salmonella in the laboratory. And I call that my "couch potato Salmonella." We get information on what Salmonella grows on, how it acts, the pH, environments and stuff, based on how it grows in tryptic soy broth, in a test tube. That's not the environment that Salmonella lives in.

Salmonella lives in the gastrointestinal tract. It's a very hostile environment. Hundreds and hundreds of other species and strains of bacteria that are interacting with it, trying to create a hostile environment for it, but yet it seems to still survive. A lot of the things that Salmonella needs to grow on must be down there. What are the nutrients that it needs? How can we target intervention strategies against Salmonella by manipulating the gastrointestinal tract system? I call that microflora management. Salmonella and other enteropathogens are, of course, from the gastrointestinal system, which we still know very little about.

We've done some work in our laboratory trying to model the GI tract of chickens, and we used a continuous flow culture, which is a simple machine. I'll show a cartoon of it--to compare the survivability of Salmonella typhimurium in the ceca of the chickens, to what goes on in a

continuous flow culture of cecal bacterial, where we know what the population of bacteria is.

And this is what a continuous flow culture looks like, and basically it's a reservoir here, where we put in microorganisms, in a medium, and then pump at constant rate a medium through here, and we can maintain, under stable conditions, large populations of microorganisms. And we can identify the microorganisms, and we know what they are, so that we can look at interactions between those microorganisms and Salmonella.

Now, we just did a really simple challenge study where we challenged chickens, and we challenged the in vitro model to see if the survival of Salmonella compared, between live animals and in the model itself--to see if we could actually develop a model that we could use. This is the clearance rate of Salmonella typhimurium in the in vitro model. We've challenged with about 10^5 colony forming units per mil, and it's very predictable. We have done experiments from 10^1 to 10^6 challenge, very predictable length of time that it takes for Salmonella to enter or to exit the ecosystem. We've done this time and again, and these are the type of numbers that we get. We can say that if we give 10^5 Salmonella into this ecosystem, it takes about four days for it to clear.

The problem is, if we challenge these models with 10 to the sixth, Salmonella hangs around the environment. It goes down to 10^2, and it stays in these continuous flow culture models forever. Every time we've done the experiment we've had the exact same data.

So what I would like to know is: how is this Salmonella different from this Salmonella? And what information can we use on that to try and get rid of that Salmonella?

This is a busy slide, but just some data here shows you--compares what happened in the chickens to what happened in the continuous flow culture. And, basically--I'm not going to go through this to any great extent--but the fermentation parameters in the chickens and the continuous flow--the in vitro model--were similar; all the parameters. The pH was very much the same, but we had--the important thing is, we had the same thing happen in the chickens as we had happen in the CF culture model. When we challenged chickens with up to 10^4 Salmonella colony forming units, the chickens were able to get rid of the organism. However, when we challenged with 10^6, we have low levels of Salmonella that stuck around.

So we verified that the model may be very worthwhile to look at things with.

So using that, we went ahead and we developed another continuous flow culture model, where we looked at microorganisms that we put in there that had been exposed to chlortetracycline. We got the cecal contents from an adult pig that had been fed chlortetracycline for several months.

This red line here depicts the time that Salmonella would take to flow through the *in vitro* model if it was neither growing nor dying; it was inert object. This green line here is the amount of time it took for the Salmonella to clear through a culture of microorganisms that had been exposed to chlortetracycline. You can see it took four days. Animals that had not been exposed

to chlortetracycline, and the *in vitro* model there, microorganisms it only took three days.

So we show yes, there is an impact of antimicrobials on the resistance that the normal flora can confer to an animal. So this is worth looking into; looking at other antibiotics to see exactly what impact do these things have on the normal flora and their ability to protect against Salmonella colonization.

Other things that we've learned in our work over the last several years: the impact of current production practices on CE efficacy. What are the impacts of weaning? We know that we can sort of protect an animal through there, but if we give a CE culture to a young animal and then don't support him through the weaning process, we know that the efficacy is decreased.

Another thing that we are very concerned about is the practice of molting, which is basically feed withdrawal. Dr. Corrier, in our laboratory, has published a paper recently showing when we molt animals, we deprive them of feed, the number of anaerobic CFU's in the gastrointestinal contents, the bacteria in there, decrease and that animal becomes extremely susceptible again to Salmonella colonization. It's a serious problem.

What are the effects of feed withdrawal, of transportation, antimicrobials and the effect of diet? These are the type of questions, I think, that we need to answer. And these are not going to be solved with competitive exclusion. These are going be solved with other types of intervention strategies, along with competitive exclusion, perhaps.

These are some data that Dr. Corrier, I think, has just recently published on the comparison of Salmonella in the crops and the ceca of broiler chickens before and after feed withdrawal. Earlier in my talk I mentioned before animals are live-hauled for processing, we pull up the feeders, they go without feed for four to eight hours, depending on the particular producer. During that time, we know that Salmonella, other enteropathogens, are re-introduced into the system. What is the amplification of that during feed withdrawal?

Here's the crop, which is the first reservoir: 1.9 percent of the chickens had Salmonella in their crops prior to feed withdrawal. After feed withdrawal, that was increased fivefold to around 10 percent. Within the ceca, really not much impact.

So the crop is a very important critical control point. We need to know how to decrease this amplification during feed withdrawal if we're going to still withdraw birds from feed prior to processing.

What about Campylobacter? This is the effect of feed withdrawal on Campylobacter. Within the crop, once again: 25 percent of the birds were positive for Campylobacter prior to feed withdrawal. After eight hours of feed withdrawal--and I believe these were eight-hour feed withdrawals--62.4 percent were positive. In Don's actually paper, he shows how it goes up over time.

Within the ceca, once again: 1.3 to 3.8, still very low levels of Campylobacter were in the

ceca. So it's identifying the crop as a critical control point. Within the poultry industry, we need to address and develop an intervention strategy to work during this time.

Using our models, we've shown the effect of nutrient withdrawal on anaerobic CFU's from the contents taken from a mature cow. Cattle, generally in their rumen, which is the foregut--the chamber, the big fermentation chamber--they generally have a population of around 10^{11} anaerobic CFUs in there prior to feed withdrawal. When you take nutrients away from this population, you can see here, very rapidly, within 24 hours, we went from 10^{11} down to below 10^{8}, nearly 10^{7}; nearly a four order of magnitude reduction in the protective flora which is in there. And then we re-fed the model--put nutrients back in--it went back up very quickly.

This is what happens to E. coli 0157:H7 during the same time, when we challenged these models with E. coli 0157:H7. We challenged with 10^{7}, and within 24 hours, really, we're going down less than half a log. So if you look at that quantitatively, at time zero, when we challenged, when we have 10^{11} anaerobic CFUs of normal flora, we put in 10^{7} E. coli, it's .0001 percent of the population. After 24 hours of feed withdrawal,E. coli now represents 50 percent of the population of the bacteria in there.

When we re-feed that fermenter, we can see that the protective flora come back up and E. coli goes way over a period of several days. So it's, once more, an example of: we need to be able to develop intervention strategies to manage the microflora in animals if we have any hopes of creating a barrier effect in the GI tract against pathogens such as Salmonella.

And here's just the two on one graph. We have feed withdrawal, anaerobic CFUs go down; E. coli really doesn't do much. When we re-feed, E. coli begins to go away.

What else do we think we need to do? Well, we need to develop CE cultures, or other types of microbial intervention strategies to be used as a therapeutic for treatment of pathogens. Currently, competitive exclusion is simply only a prophylactic treatment. It will protect animals from getting Salmonella, but if you already have an animal with Salmonella, don't spend your money on competitive exclusion; it doesn't work that way.

However, using models, we would like to increase our knowledge of the pathogen, host, and normal flora interactions so that we may be able to develop a new intervention strategy which is not an antimicrobial. And that's why competitive exclusion or some type of microbial intervention strategy--I think that the word is out, and I think it's coming, folks--that somehow or another we have to decrease our dependency on antibiotics in our production.

This is just an example of how CE does not work. And I work in the competitive exclusion area, and I wish it worked here, but it does not. And you have to be honest about your technology and know what its limitations are.

These are control animals that are infected with Salmonella. A hundred percent of those animals or birds become positive, and we have cecal content concentrations of around a million

Salmonella per gram. Now, if we wait one day before we give the competitive exclusion culture, eight days later, 93 of those birds are still positive for Salmonella. So competitive exclusion does not work as a therapeutic. It's only a prophylactic. And if we're going to develop something that is not an antimicrobial-based intervention strategy, we need to understand more about what goes on in the GI tract.

Competitive exclusion in any type of intervention strategy is going to be simply one part of an integrated program to prevent or control Salmonella in broilers. We need to go to the broiler breeder flocks; we need to be able intervention strategies at the hatcher; we need to stay at it in the broiler grow-out; we need to look at transport; we need to clean our live-haul crates; and we need to develop better processing technologies in the processing plant if we have any hopes of getting rid of this pathogen in our food producing system.

One of the things we need to do is we need to put products to our producers. One of the concerns that I always hear from people is: we don't have any products. We spend a lot of time looking at how big the problem is. Give us some tools in our bag. And this is just one example of a product that was developed by ARS, but we need many, many more.

And this here is--it's a chicken from Texas, you can tell, because it's got a gun, and even our chickens in Texas have guns.

But, anyway, what we need to do is empower our animals, our chickens, or whatever, by developing new strategies so that they can protect themselves against things like Salmonella.

Thank you very much.

Management Interventions:

II. Beef and Dairy Cattle

DR. HANCOCK: While I'm getting warmed up here, I'll tell a pre-harvest food safety joke. And Beth, I'm sorry, it's about pigs. We don't joke about cattle in the west.

[Laughter.]

Back several years ago we had a lot of surplus apples in Washington because of the alar thing, and some of the apple growers took to growing pigs, and one day this new WSU graduate was out driving through apple country and he saw this apple-cum-pig-farmer feeding his pigs apples. And he would pick one pig up and hold it up to the tree and let it eat some apples, and set it down, and pick another pig up. He did this for awhile, and the young WSU graduate walked over to the fellow and said, "You know, it'd save a lot of time if you just knocked those apples down on the ground and let the pigs eat 'em off the ground." And the old apple farmer looked the young graduate in the eye and said, "What's time to a pig?"

[Laughter.]

So I'm going to talk to you about pre-harvest food safety interventions on cattle farms, and most of this stuff will have to do with E. coli 0157. In fact, all of it may have. I had, like, 20

or so other slides at the end on Salmonella, but we probably won't get to them.

I just wanted to recognize my colleagues, and particularly I wanted to emphasize these with APHIS Veterinary Services. We started a collaboration under Dr. King's administration that has proved to be extremely fruitful.

Why should we be concerned about E. coli 0157 and other pathogens on farms? Because, as several speakers have pointed out, that ultimately is where at least a lot of them in the human food supply come from. And this is just an example of a couple of different studies. The data from feed lots is from a study that was done under the NAHMS system, in which we participated, and then the holding pens and the post-mortem collection is a study that we did in several slaughter plants.

And so you see a hint of an increase is not significant, but the key thing is that we don't have to speculate about where E. coli 0157 in a slaughter plant might come from. There might be other sources, but certainly most of it would come from cattle.

And this--the bars are fecal prevalence but, perhaps more importantly, we have these things called "dung locks"--or some people call them "tags." Or, in Australia, I was curious to find out they call them "dags." And we found it in 1.6 percent of those, and we have to remember: we just collected one little dung lock, if you want to call it that. And if you look at the whole surface of that animal, the prevalence would almost certainly be much higher. And the dung lock prevalence was completely discordant with the fecal--the fecal swab prevalence.

Back to five years or so ago, I would have said a lot of people know how to control E. coli 0157, they just don't agree.

[Laughter.]

Nowadays, I think we've evolved into something--and I think we can actually thank the risk assessors for this--we've evolved into a more mature strategy where we recognize that we cannot eliminate the hazard at any single point, and we've adopted this multiple hurdle approach. So I've got the little hurdler there, where we've tried to identify places where we can reduce risk at different levels.

And I've proposed some here for the production level, but it's only been fairly recently that we were even in a position to propose some, whereas at the slaughter and processing level, there's been a lot of excellent work over the last 20 or 30 years, or even back before that.

We've just begun to understand the ecology--and there are a lot of details that we don't yet understand. And I just wanted to show you some of the complexities involved in that.

So I just want to give you a few little high points from eight years of--maybe 20 studies, to show some of the key ecologic features of E. coli 0157.

It's virtually ubiquitous in cattle populations. So notice the Y axis here is "Percent of Feed Lots." So, in each feed lot, 120 fecal samples are collected, so it's a positive if at least one of

those fecal samples are positive. The prevalence in individual fecal samples is only about 2 percent, but we found it in most of the feed lots. And, in fact, this is completely consistent with the ubiquitous distribution. If you go out on one day and sample a tiny minority of the cattle in the feed lot, and you find it in, I think, 63 percent overall--there were two labs involved in this because of the massive number of samples. And this study was done under the NAHMS project--the National Animal Health Monitoring System.

Another key feature--a very key feature--that will figure prominently--is the seasonal distributions. So you notice the red is cattle--and that's from one of our studies where we followed a bunch of herds over a year's time. And notice how closely that parallels the human prevalence, from the first few years of reporting in Washington State.

Another key feature is that there are certain groups of animals that have a much higher prevalence than others. One is the newly arrived cattle at the feed yard. This almost certainly has something to do with the gut floral disturbance that Dr. Nisbet was mentioning in other species. It's not host-specific. We should have suspected that When you colonize cattle and people, well, they're not anything alike. First flies--it's not hard to imagine how they would get it, but also dogs, cattle, horses, birds--we've also found it in deer and, actually, sheep seem to have very similar ecology with 0157 as cattle. We haven't found it in cats, but that's just because it's hard to sample cats, probably.

We want E. coli 0157 to be like a traditional infectious agent, but it really seems to be just part of the normal E. coli flora in cattle, and probably some other species. And by "normal flora," we have to specify that if we just isolate E. coli from fecal samples and sub-type them, we find many strains--maybe 50 or 100 on a farm--and a few of these, one, or two, or three--you find regularly. In fact, if you follow individuals, you'll find them most all the time. And we call these "residents." And the others--the majority of strains on a farm--we call "transients," because we only see them transiently, and they will become colonized and shed this for a couple of weeks, or a month, or maybe a couple of months, and then it's gone. And we often see a lot of animals in a group shed one of these transients together.

And E. coli 0157 definitely appears to be a transient. It's most consistent with a transient in that we don't really find carriers. We don't really find carriers. There are some animals that shed it quite a bit longer than others, but we don't find any chronic carriers with this.

And certain individuals have a less stable flora than others. One group is young animals. And that's true not only of cattle, it's true of people; it's true of mammals in general, as far as any of the studies have shown, that it's easier for a transient E. coli to invade and colonize, so there's a greater turnover of these transients. That almost certainly accounts for the higher prevalence ofE. coli 0157 in young stock. They have a three or four-fold higher prevalence than adult animals.

It likely accounts for the threefold higher prevalence in recently shipped feed lot animals.

We've done some work with using antibiotics and holding off feed, and each of those cause transient gut floral disturbance that's recognized by increased uptake of transients from the environment.

Even though we find it on most all farms--in fact, just about any farm if we sample hard enough--we see a vast range of prevalence. This is from a 36-herd study that we did in the Northwest. These are dairy herds, and you notice that we did not find it in nine of the dairy herds. We sampled 360 fecals over a six-month period in all of these. I would argue we probably would have if we would have sampled long enough. But the key thing is we found it in 27 of the 36 herds--or 75 percent--and that there was a pretty wide prevalence difference amongst those. And when an epidemiologist sees this, we say, "Well, gee, something's got to account for that." And, in fact, we designed this study to look for one particular factor, and that is the type of housing with respect to manure on grazing land.

And each of these dots stands for the prevalence in a herd, based on 360 fecals over a six-month period. And, as you see, there's wide distribution in all of these groups and no real hint of effect of manure on pasture.

However we did see something in that study that intrigued us, and we understand there are limits--and we designed it to test one particular hypothesis, and we were kind of fishing here--but we saw a variable that was most significantly associated was corn silage feeding to these heifers. And this study was done all in heifers, by the way. So we saw a significantly higher prevalence in those that fed corn silage to their heifers. And this made us think, "Well, maybe it's growing in there." We did this study in the warm months of the year--"Maybe it's actually growing in that." Feed corn silage is a wet feed. It has some stuff in it that they might be able to grow in.

And so we inoculated both general E. coli and E. coli 0157--and, incidentally, Salmonella, into a bunch of different feeds, and this just happens to be ten of them, and most of them will support a robust growth, just like if you left your potato salad out, you shouldn't feed it to your kids.

[Laughter.]

Well, I guess nobody ever really ever thought of that for cattle feed, as far as I can tell. But there's a certain amount of truth to it.

Well, a lot of cattle feeds contain a silage component, and we were interested in whether or not that silage was inhibitory. And in some cases it is. You mix an experimental extraction with a lot of silages and they're very inhibitory. They'll kill it off. But some, it grows like crazy. And the best correlates of that were the volatile fatty acid levels, in particular propionate was very negatively correlated. If it had a high propionate, it didn't grow; it tended to go down, actually. So we're following up on that relationship.

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And so here's an example of a total mixed ration for cows. It's like pasta salad for cows, basically. And you know, every time I give this talk they say, "But, yeah --but how does the E. coli get in the feed?" Well, if you would come and visit with us awhile and we'd take you out to some farms, you would not ask that question.

[Laughter.]

Because you notice that they're fed on a slab. The tractor tires that's pulling the feeder wagon go right across that. People walk through it. There's flies in it, obviously. Birds, actually--usually you'll see a line of bird manure right along here because the birds feed on it, and we've found E. coli 0157, as well as Salmonella, in that pretty commonly.

And so it's probably, on a practical level, impossible to keep E. coli 0157 and Salmonella out of mixed rations. It's probably impossible to keep Shigella out of potato salad in the fullness of time. But if we keep E. coli 0157 from growing, and Salmonella from growing, we are hopeful that it will have a major impact on the prevalence, particularly, you remember, since we see this summer peak. And the most likely explanation for that is replication in the environment.

Another possible way that feeds could get contaminated is by feeds in commerce. We have not yet found E. coli 0157 in feeds in commerce, but we do find generic E. coli in about half of feeds in commerce. And so it is a way to move E. coli around. In fact, we were interested in looking at moving resistance genes around, and certainly Salmonella occurs in about 10 percent of feeds. So, to some extent, the feeds come contaminated; they don't have to get contaminated.

Now, another area that we've worked on quite a bit is water troughs. And another at Wisconsin--Kaspar, Shere, Luchansky, and others have done a tremendous amount in this area, too. This is a water trough on a dairy farm, and I've labeled on the wall there, like it's written on a wall, "Hard to clean. Easily contaminated."

In fact, just think of yourself cleaning that trough. How do you do it? And this is not the hardest trough to clean that I could show you. This just happened to be one I had a picture of. Some of them are set in concrete. In fact, E. coli 0157 will persist in these troughs for at least four months. It will grow in the sedimentary layer that's there.

And on dairy farms, water troughs are frequently never cleaned. Here, with our highest category--and this little survey was "greater than a year." We should have had, like, "in the lifetime of anybody now alive", but a majority of them had not been cleaned in the last six months, as you see.

And another key thing is the counts of E. coli--generic E. coli, here--increase in the summertime, consistent with replication in that environment.

Now, this is similar to what the Wisconsin group has published recently in Applied and Environmental Microbiology under first-author Shere. But this is some of the data from one of our University herds, showing the concordance of water positivity and animal positivity.

And so there does seem to be--it's hard to pick out exactly which way it's going. Maybe the animals contaminated the water because they're shedding a lot of it. They're not very hygienic, you know. But at the very least, water's playing an important role in dissemination, we think.

Now, the situation on feed lots is different. You know, for all the abuse feed lots take, it's a rare feed lot that doesn't clean its troughs once a week, or they at least target once a week. They might slip somewhat.

But I think this shows that even though it's a simple concept to clean water troughs, operationally it's very difficult to control what we're trying to control. This shows the mean of 10 water troughs; the pre-stir counts, you notice, are 5.3 CFU per gram; the post-stir is 328 CFU per gram. And so you get a sense that there's something going on in that sedimentary layer, right? And, in fact, that sedimentary layer in a feed lot water trough is a lot of feed, because it sticks to their mouth, and they go and drink out of there, and it actually forms a little colloid in the bottom of that trough; or it looks like a colloid. I don't know if it meets the technical definition, butE. coli will grow in that.

In fact, we did an experiment--we did one in the spring and then in the summer, on how often you would have to clean a trough to keep those counts down. In the spring it looked pretty good: like every four days, maybe, you could really keep them down. In the summer, the troughs that were cleaned 24 hours ago had as high a count as those cleaned seven days ago.

And you notice, they're made for cleaning. You see this little plug here, and its nice sloped smooth sides. So the feed lots have water troughs that are made for cleaning, but probably not cleaning three times a day. So you probably had trouble training your dog not to drink out of the toilet, but maybe your dog's really a lot smarter than you think, because what we need is, basically, to get rid of that sediment; to have a self-flushing trough.

And I predict that in five years we will have a totally different kind of water trough than we have today.

So just to look at the possible levels of on-farm control, you know we'd like to eradicate, but here we have something that's basically ubiquitous; present in wildlife. We're not going to eradicate it.

We don't really even know how to establish bio-security in these herds. So we need to look at some ecological measures; animal feed safety, particularly with respect to keeping it from growing. Water safety--so keeping it from growing and persisting. And then factors affecting host susceptibility: one area in particular I'll mention is competitive exclusion, because here we have an agent that is more common in young animals because of the decreased gut floral stability. It's more prevalent in recently shipped animals because of decreased floral stability, and so it seems to be a logical target for competitive exclusion. And I know Dr. Doyle's group at Georgia has done some work in that area. And so I think that merits following up further on and hopefully

getting some more funding.

I was walking out across a feed yard with the nutritionist one day, and he pointed out to me, "Look at these cattle; they're eating dirt," you know. And I think --which animal is it? One of these in the background is eating dirt. I took a picture of it. And, obviously, they live in a certain amount of filth; that's why we say "living like an animal."

And, you know, he was skeptical of all of this stuff, that it would really have an impact if we looked at feed and water. So I completed this little spread sheet, in fact, this is not even the highest levels we've seen in water, but it goes out to maybe on the 90th percentile, and then the levels that we naturally see on farms in feeds, and, you know, we summed them up, and notice that at the higher end of that you get really high intakes of genericE. coli, in this case. Certainly, at the extreme levels, this must account for the great majority of their total enteric bacterial flora. We haven't really done a lot of counts of the dirt they ate off of the ground, but the counts in feed, at the extreme, can get as high as what is likely to be in that dirt.

And so our goal of these efforts, I believe, is to ultimately try to chop the peaks off of that, or at least--maybe not quite as good as what it looks, but at least chop some of the peaks off.

This is the human reported disease for a three-year period. This same pattern has been reported in Great Britain, by the way.

Now, it wouldn't be complete if I didn't mention a recent article in Science I'm sure a lot of you are familiar with--Diaz, Gonzales, et al.--that reported that if you could switch feed lot cattle to hay five days before shipping, you could greatly reduce the 0157 prevalence. And that's based on the fact that grain feeding causes increased VFA in the colon--volatile fatty acids--and decreased pH. And so switching them to hay lowers the VFA levels and the pH becomes more toward the basic end.

And E. coli exposed to mild acid environment are made acid resistant. And E. coli with induced acid resistance are more likely to make it through the low pH of the stomach.

So the first two--certainly, the first one was known before this paper, and the second one they did a reasonable job, at least for generic E. coli; they didn't really look that much at E. coli 0157. The third one is a hypothesis that's a reasonable hypothesis, but one for which there are no dose-response data that I'm aware of.

Now, I think it's worthy of note to look at this last sentence in their paper, because I actually took considerable exception to that: "Our studies indicate that cattle could be given hay for a brief period immediately before slaughter to significantly reduce risk of food-borne E. coli infection."

This is a case where it was a really neat idea, and it's an important contribution. But by testing this one little hypothesis about acid resistance, they assumed a whole lot of other things were true and, unfortunately, those whole lot of other things probably aren't true.

So here are the problems that our little group sees with this paper. STEC, including 0157, are typically acid resistant without exposure to mild acid. People rarely eat E. coli from the colons of cattle.

[Laughter.]

The source of most bacterial contamination on a carcass is the hide and hooves. Surely, these probably share an ancestry with the bacteria in the colon, and maybe their ancestors departed the colon at some point, but in the warm weather in particular, there's almost certainly some environmental replication. And also much additional contamination occurs in the breakdown from the little nooks and crannies, from the E. coli that multiply there.

And then, also, there are at least a couple of papers by KUDVA, which were not quoted in this Science article, that indicated that the proposed action--switching to hay--causes an increase in prevalence of 0157. And there's also the potential to increase the prevalence of Salmonella. In fact, it's a very real possibility, although it hasn't been examined.

Are we out of time? Let me show the last slide, and then I'll quit.

I'll just show my assessment of the research needs.

So we need more detailed work on the role of water, feed and dietary management--the ecology of enteropathogens. We need more funding and research for competitive exclusion--or "inhibition" really is the better term.

We need--I didn't get to discussing this, but we definitely need some work in the role of commercial feeds and byproducts in the dissemination of enteropathogens and antimicrobial resistance genes. And then, as several people have mentioned, we need broad efficacy studies for specific strategies. And then we need studies on the role of different sorts of antimicrobial uses in livestock in the emergence and dissemination of resistant pathogens.

So, thanks very much.

[Applause.]

Discussions of Papers

DR. KING: Let me thank the panelists for some very insightful comments--even entertaining, Dr. Hancock.

I hear stomachs growling out there, but we have about five minutes or so. If there are questions, we can entertain them now.

If there are, please go to the microphone so we can get it on the record. You're not that hungry, are you?

Let me ask one.

Dr. Lautner: You put forward a group of priorities for NPPC. How do you ensure that priorities and needs for research that your organization have, and for the swine industry, are met by the Federal government?

DR. LAUTNER: That's a good question and, actually, that brings me an opportunity to point something out that, I think, as people look at different groups' research priorities, sometimes--and I would say this is probably true in the case of ours--some of our priorities, or what may be seen as a higher priority, are really more related to applied-type research; research that answers questions more directly. It doesn't mean we don't support basic research, because we do. But we recognize that there are Federal agencies and other groups that maybe take on the longer-term type projects, and producers are more apt to want to put their money into some shorter-term type issues.

So I think that's very important, when you start looking at different people's lists of priorities, to understand the context that they've set those up in; and, in our case, the other thing we've done is try to identify gaps--where we saw a gap. So we may actually fund research in something that's a lesser priority to us than something maybe the Federal agency is funding, but we see it as a research gap that's not being addressed.

So I think all those things need to be taken in context. And we, through our working groups, bring in ARS researchers, CSREES attends those, and you're able to try to collaborate, and try to--on our review panels, as well--try to have representations from Federal agencies that are doing research so that we're not duplicating research and we can make sure that we're maximizing our research dollars.

DR. KING: Thanks.

Further questions?

And we'll reconvene at 1:30 for the next panel.

Thank you.

[Lunch recess.]

[Whereupon, the meeting was recessed, to be resumed at 1:30 p.m.]

A F T E R N O O N S E S S I O N

SESSION III

DR. WAGNER: Good afternoon. I'm Bill Wagner, and I am a National Program Leader in the Cooperative State Research Education Extension Service.

One item that I want to mention to you is that later today there is a reception that is being sponsored by the National Alliance for Food Safety. It will start at 5:30, and not 6:00 p.m., and it will occur in the room immediately adjacent to this one: the Washington Room. So you go out in the hallway and back in the next door.

I'm going to keep my introductions of the speakers very brief, and I will introduce each of them as they come in turn, rather than doing it all at the front end.

Our first speaker is Nancy Nagle, who will be talking about the fresh fruit and vegetable produce industry. She lives in California and is a special consultant on food safety issues for the United Fruits and Vegetables Association. And I told her I would not give a long pedigree--so, Nancy, you're on.

Fresh Fruits and Vegetables Industry

DR. NAGLE: Okay. Thank you.

I decided that since we've just all come back from lunch, I'm going to move around to make sure you stay awake and don't have the opportunity to doze off.

Just to head it out a little bit, I am speaking on behalf of the United Fresh Fruit and Vegetable Association today, with our comments on what the research needs that we see for this food safety arena.

A little introduction: United is a trade association that represents the produce industry. It represents the growers, the shippers, the distributors--essentially the producers of fresh produce. I want us to all think about this. We talk about "produce," and we use that word--one little word, right? Now, think about the produce section in the grocery store. Lots of little things. Lots of stuff. It's not like even talking about meat, or poultry, or dairy. I mean, you think about it. Meat is meat. It's muscle tissue, and it comes from different sources, or whatever, but produce, when we talk about it--produce is leaves, stems, roots, berries, seeds, and any other part--I think I've used up all the parts of the plant. So it's not a ubiquitous--or it's not a homogenous kind of a product.

So when we talk about "produce" we have to keep in mind that it is a very, very broad category of food, and we don't want to lump it all into one area.

We also know that there's been huge benefits to the increased consumption of fresh fruits and vegetables. The industry and the government together, and the Public Health Service--have been pounding out the five-a-day message for a number of years, and we feel like we're being successful there. We don't want to put a halt to that, because we do think that the benefits of

produce consumption far outweigh some of the risks that we've talked about today, and we want to make sure that consumers don't use it as an excuse to stop eating fruits and vegetables.

We do know that there is some epidemiological evidence that associates produce with food-borne illness. And that's been presented today. We heard Bob talk about that, and we've seen a number of other references to that. We're not saying that it's not an issue, but what we are saying is: let's not overreact, and we need to focus on the real issues in the produce.

One of the areas that there's been a lot of suggestions about is a need for an extensive survey of the industry to find out what's going on and what's out there. And we think that's a great idea except, again, as I talked about the broad produce industry as whole. If we go out there and decide we're going to do this sampling to find out what the extent of the problem is, that's a pretty daunting task, as far as sampling. You're going to need to sample over the time course of a year, at least, so that you get all the different growing areas accounted for, and then you want to do it for each of these individual type products. And when you start multiplying and putting all that together, the amount of effort that would be required to go into an extensive survey kind of research like that, I don't think--we don't believe would give results that are actionable. The incidence is so low that you'd have to have such a high sampling level that--to find the organisms and to really get a good read on it, that we think that our money could be better spent in more of the prevention-type methods which I'm going to talk about, and which we've heard some of already today.

So, United, on behalf of their members, want to put forth our recommendations for where we think research needs to be done. And our first category--the first area that we want to talk about--is water. We think there is a real need for increased research on the impact of water source on produce safety. We've heard that those questions have been asked, and we think that's an important question to follow up on.

We also would like to encourage more research on the irrigation methods, and which irrigation methods are either promoters of a problem or which are methods that could prevent development of problems.

We also think that there needs to be more research in the area of cooling and handling methods on pathogen reduction. Are there certain methods of cooling that can be used that show a much more dramatic decrease in surviving pathogens than other cooling methods that could be employed?

A very important criterion--and one that growers keep asking about, and people at the end-user--you know, the guys that are the ones that have to actually implement --keep saying, "Can you define what kind of microbiological testing parameters are appropriate for water? What are the indicator organisms we should be using? Then tell me their critical limits, and give me an intervention strategy if I exceed those limits." And we think that that's a really important question

that's been raised.

Another area of concern is: we know that in a lot of operations in the agriculture arena water treatment is used. I mean, we use chlorine. There's a lot of chlorine used in cooling. But we also would like to know what are some other water treatment possibilities: ozone, organic acids, peroxide, chlorine dioxide. Which of these treatments are the most efficacious? And maybe certain ones are more effective in certain types of applications, and we really feel that we need a lot of help on that area. We want to see more research along those lines.

Another one of the discussions this morning was based on a lot of talk about risk assessment. And we couldn't agree more that there needs to be a lot more effort into the area of risk assessment.

One of the questions that we think could be answered--should be answered--in order to help with this risk assessment is get some more information on the microbial ecology of the growing of produce, and in the handling environments and in the growing environments for produce--probably, especially for E. coli 0157, Cyclospora, and any other food-borne pathogens that have been associated with fresh produce. But we really feel that getting a better understanding of this will help in developing strategies.

We also feel that we need to know where is the contamination most likely to occur. And I want to just bring out one issue that we've talked about. A lot of times we hear about a produce-related outbreak. And this is not to say that we do not want to take responsibility for the things that the produce industry is responsible for, but when you hear about a produce-related outbreak, often you then hear, somewhere along the line, about some other cross-contaminating event or occasion that's tied in with that.

An example would be: there was a lettuce outbreak in a Boy Scout camp in Maine. It was associated with lettuce, through the CDC--rightfully so, because all the people that ate the lettuce. But the problem was that the lettuce was stored on a shelf under raw hamburger meat. The raw hamburger meat juice dripped onto the lettuce; the camp people didn't wash the lettuce well enough before they made salad and used it on the food. So that incident is tied to lettuce.

And we need to understand where in the supply chain these contaminations are happening, because all the efforts that a farmer can put in are not going to make any difference if the end-use--if it's happening at that point in the chain. So we need to make sure that we're putting our efforts at the right points in the production chain.

Another question that we feel needs to be asked is the determination of infective doses for these organisms so that we can understand, again, how to manipulate critical limits, and what should be done with food products that either exceed these limits or are not within the recommended levels.

We also need to be keeping in mind--and I know this is, maybe, policy or something else

that's an issue--but we need to keep in mind the balance of the risk from consumption of getting food-borne illness, along with the benefits to lowering of chronic diseases, such as heart disease and cancer, and not get out of balance on that area.

Our members have also asked that we look into cost-benefit analyses. We want to make sure that we are spending our money appropriately on interventions and on strategies that will result in the greatest benefit for the least amount of cost. Again, it's not saying that our members don't want to spend the money, but they don't want to spend the money in a frivolous manner; they want to make sure they're addressing the appropriate problems.

Manure has been raised by several people as a potential source of contamination. And we agree there needs to be a lot more work with that. It seems very logical. You talk about it, you look at it, and you say these animals can be carriers of human pathogens, and therefore, when the organisms are shed, it ends up in the manure.

Well, some really key questions need to be asked. There's 1.3 billion tons of manure produced annually in the United States. And with that quantity of product being produced, it needs to be used in production agriculture. We can't just, you know, stick it in landfills or something. And it's a very valuable resource to the land. It's been very helpful. It supplies organic matter. And for farmers, this is a very valuable tool.

So what we need to do is have some research conducted that will help us understand what constitutes the safe use of manure. Does it have to be composted? Can it be used as a pre-planting treatment? Can it be used in late season treatments and then, with long spaces before, used as raw manure? All of these questions need to be asked.

Again, then, if we find out that composting is what needs to be done, we need to know what are the indicator organisms that we should be looking for. Again, this is a grower, or someone who's out there in field. He can't be running extensive microbe testing. But if he was told, you know, "You need to run an indicator," or test--you can test for X organism to see if your process has been effective, this would be very useful. This would be very helpful.

And, again, what we'd also need is some critical limits so that we can tell people what levels they should be shooting for.

And then, again, one other issue that we've asked for is what treatment is required to achieve this limit. And then all of these--are there different effects of different manure? So, does chicken manure respond differently than cow manure than sheep manure?

We have just a couple other issues that we wanted to talk about, and that was just to evaluate handling practices; the effects of humidity and temperature combinations on pathogen control on survival in whole fruits and vegetables. There's been a lot of work; people have been looking at pre-cuts, but let's look at the whole fruits and the whole vegetables, as well.

We also would like to have some identification of novel ways users can prevent or

eliminate pathogens from fresh produce; things that could perhaps be used at the home or at the restaurant level.

We are looking for worker hygiene and sanitation programs and a determination of the impact of worker health on safety. We talk a lot about it. We need to have a little bit more facts so that helps us in going back to unions. You know, one of the big issues--we can talk a lot about worker safety, and worker hygiene and these kind of things, but a lot of that--a grower is dealing either with a unionized workforce, or a non-English-speaking workforce. There's a lot of issues with this. And we can't just say, "Oh, we'll make them do it." You can't always do that, especially if you have a union.

So you have to be able to explain why it's important, and then you can get these things accomplished.

We've asked just that we continue--and I heard someone this morning talk about, you know, let's not forget basic research, and let's not forget some of those things. We still think there needs to be a lot of effort into the area of new technologies: UV, ionizing radiation, pulsed energy, ozone, gas-based disinfectants--any of these kind of things that can be effective in helping to reduce microbial load and improve product safety.

I think I've stayed within my time--and thank you.

DR. WAGNER: Thank you very much, Nancy, for that nice overview of the fruit and vegetable industry needs.

Our next speaker is Dr. Ed Cleveland. I will be happy to take credit for the "Ted" in the program. It's supposed to be "Ed" Cleveland. He is the research leader for Food and Feed Safety Research Unit, the Southern Regional Research Center of ARS in New Orleans.

Dr. Cleveland will talk about mycotoxin occurrence and prevention during growth.

Mycotoxin Occurrence and Prevention
During Growth

DR. CLEVELAND: Thank you, Bill. I've been called a lot worse than "Ted" so that's all right.

Let me start out by saying I really appreciate the opportunity to provide my opinions--as a research leader, and also as a bench scientist--on exactly what are some of the research needs in the area of mycotoxin prevention.

My talk, which is entitled "Mycotoxins Occurrence and Prevention During Growth," will be broken down into two sections. I'll briefly, in the first few slides, talk about what is the relevance of these mycotoxic problems to agriculture, and then I'll spend most of my talk on research needs for preventing the problem to begin with.

But I think it's important to just show you some of the information on what are the major crops affected, the toxicological aspects and economic losses. Because this points toward, really,

three groups of mycotoxin-producing fungi that I think we need to enhance our research in.

And then just briefly I will discuss current research, but only insofar as some of the current research that's going on has given us some important leads on where we could really enhance the effort to control these problems.

Well, mycotoxins are natural products. They're produced by fungi. They produce a toxic response when they're introduced in low concentrations into higher vertebrates and other animals.

And, as I said, in this talk I'm going to focus on three groups: the ones produced by Aspergillus flavus and parasiticus--which makes the aflatoxins. These are generally toxic, but what really concerns people is the fact that these are mutagenic and carcinogenic. Fusarium moniliforme makes the fumonisins. This is a recent concern. This really concerns the corn industry. The toxicology of this is that it causes a lesion in the brain of horses called leukoencephalomalacia. Whether it's carcinogenic or not, the story is not quite in on that yet. There's a major study going on. The result will be in pretty soon on that, but I can't say much about that at this point. It also causes a serious lung edema in certain livestock.

Fusarium graminearum is another major problem. It produces two toxins: deoxynivalenol and zearalenone. The first causes a digestion disorder, like vomiting, nausea, feed refusal and diarrhea. The second one, interestingly, is estrogenic, and it can cause reproduction losses in livestock.

Now, if you look at the crops that are affected by these toxins you can see that these two groups of toxins--the ones affected by aflatoxin, and the ones affected by the fusarium toxins--cover an awful lot of the very major economic crops in the U.S., including corn, cottonseed, peanut and treenuts. The fusarium toxins cause problems on corn and wheat and barley. So, geographically, these things are the major ones. They cover practically all the major crops in the U.S., between these three groups of toxins.

And when Aspergillus invades corn, you get very high levels of aflatoxin and this, of course, makes the corn unsalable when it occurs at very high levels.

And just to show you a little something about the head blight--or "scab," it's called--of small grains, this shows the symptoms on head scab of wheat and on barley. It causes a reduction in the chlorophyll or chlorosis and these kernels will be shrunken. So you get a yield loss, as well as having the problem with these toxins that are carried over into the kernels. And the same thing applies with barley.

So, to make a long story short, the economic losses are just tremendous. In the case of aflatoxins on the major crops, between 200 and 300 million has been estimated in a year of a severe outbreak, like when you have a drought in the midwest corn belt, for example, that effects corn, because that is where you get your major losses.

As far as the Fusarium toxins on wheat and barley, this has amounted to over $3 billion

over the last six years or so or, at least, between '91 and '96. So economically, these are a terrible crop and also a problem with food safety.

So, I think in these first few slides, you can see the relevance of these toxins to agriculture, both from a food safety and from an economic standpoint to the agricultural industries. So, let me say a little something now about what kind of research do we need in the future to try to prevent these problems.

Well, first of all, philosophically and based on practical information, we think that elimination of preharvest mycotoxin contamination is the way to go, rather than have to deal with it after harvest. So, in other words, interrupt the process before harvest. This is where I think the research should head, in my opinion. There are some new approaches out there that are basically coming to maturity as far as control of other plant diseases. They have not been applied as much as I would like to see on the mycotoxin-producing problems.

For example, biological control and host resistance, these are environmentally benign-type technologies and I think they should be enhanced through research. Let me mention a little something about plant breeding, because there is some new technology out there for plant breeding.

One area that we really need to know more about or a couple of areas really are, what are the traits that limit fungal growth. We need to know this kind of thing for the plant breeders. There are also traits, interestingly enough, that may be involved in limiting the formation of the toxins and the biosynthesis of the toxins. There may even be traits that can detoxify mycotoxins.

So, for breeding purposes, we need to do more research on identifying these traits. To do this, we need to know more about the pathology. We need to do more research on what is the pathology of the disease process caused by these fungi. One way to help this is using some new tester strains of fungi that you see here.

This is an Aspergillus strain that has a reporter gene in it. You can study the disease process by tracking this blue color, because the gene that is in there gives it a blue color during invasion. You can track the pathology, how it enters the plant. Is the plant able to resist the attack? That way, you can really determine the disease mechanism that is going on.

I think this could be expanded to some of the other mycotoxin problems as well, to study the pathology on wheat and barley, for example, caused by the Fusarium. Using this technology, scientists were able to identify some resistant inbreeds. You can see the fungus has started right there, but it can't spread any further.

This is a non-commercially valuable inbred variety that was screened using this technique. It turns out that it is highly resistant, but it is not any good as far as yield. At least, there is hope for the locating of resistant genes out there, which could be used in breeding.

Now, as far as that trait for resistance goes, what is that trait or traits?

mgs

Well, one place where information is beginning to come in is that these seeds containing proteins are antifungal. I suspect they are not only in corn, but they are also in wheat and barley. They could be the markers of the future that plant breeders can use to select for resistance.

There are also some very interesting chemicals, which are volatile in nature, that are produced in corns and some of the other crops like tree nuts. Some of these are, for example, insect pheromone synergists or insect attractants. These were discovered in tree nuts.

This is important because insects injure crops and predispose the crop to attack by these fungi, which get in through the insect injury port. There are fungal growth inhibitor volatiles and also, interestingly, there are some of these compounds in plants that inhibit the pathways by which these toxins are biosynthesized.

So, if we can learn to manipulate these volatiles, perhaps through genetics or plant breeding, it could go a long way toward interrupting the process by which the toxins get in the plant. We are just at the tip of the iceberg here. This needs to be expanded.

In fact, lately, there has been a whole variety of plant metabolites that have been discovered that we have found that can modulate, either stimulate or repress aflatoxin biosynthesis. These have been discovered in corn and tree nuts and some of the other crops. These are the markers that a plant breeder could use, if they are identified.

This is a DNA analysis gel, which you might see in a crime lab somewhere, but we are not trying to find a criminal here. We are looking for a resistant variety of corn. Each of these lanes represent the DNA profiles of different varieties of corn. What the breeders need is for us to begin linking some of the unique bands that are associated here. You can see; they are not all the same.

If we can learn to associate unique bands with resistance, then these provide very good markers that a plant breeder can use in their selection process to come up with commercial varieties. Also, if the DNA band for resistance can be identified, for example, you might be able to find what are the genes that are responsible. This could lead to genetic engineering technology.

Based on the data that is coming in, preliminary data, there is more than one trade involved in these types of resistances. These are not single gene type resistances. They are probably multiple genes, which makes it very difficult for plant breeders. There is probably a regulator or a regulatory gene involved for turning on these genes. Really, we need to find out what these genes are. We need more work done on the genetics of how these compounds are produced in the plant for the breeder to be able to exploit them.

Finally, if antifungal gene proteins or other type substances can be identified in one crop like corn, there are likely to be homologues of those genes in the other grass family, like wheat and barley. So, I think we need to begin comparing notes between the people looking at these different crops, perhaps through a shared database. As the information comes in, there may be

analogs of these same traits in the other grasses.

Now, the advantage of plant breeding is that it's a natural way that you can develop resistance. However, genetic engineering offers some possibilities in that you can transfer a single trait at a time. The problem with plant breeding is that, when you breed plants, you are really transferring more than one trait. Many times, some of the traits are not desirable for a commercial variety. So, this is a very attractive technology as well.

To summarize, I can say that, every one of these crops has been genetically engineered in the lab, but it is not a very efficient process. It is not very practical in some cases for a lab to do this, but it has been done.

In the case of cotton, for example, we have done this in our group. We have transformed cotton cells with genes for antifungal genes. These can be cultured. If you put them on the right combination of hormones, you get embryos. These embryos can be germinated. You can end up going from a culture into the greenhouse and into the soil and into the field, but this is very laborious. There is only a handful of people in the country, in the world who know how to do this. The same thing applies with these other crops as well.

It is not an efficient process. We need more research so that we can transform commercial varieties. A lot of times, these are very special varieties, which work well for genetic engineering, but they are not commercial varieties. So, they are not the high yielding types that you want. So, that work needs to be enhanced.

If we can develop efficient ways to transform plants, it offers the possibility of transforming plants with a variety of genes, including insecticidal proteins, which as I said, insects can vector in these problems, antifungal proteins and even mycotoxin detoxifying enzymes. There are some antifungal genes out there. There are not many of them. We have tested a few of them using tobacco as a model system, which is easy to transform.

The middle leaf is diseased with colletotrichum, which causes a lesion. The ones on the left and right were transformed ironically with a gene that came out of a resistant line of corn. The protein that I talked about has been cloned and this was put in tobacco and it, indeed, embellished tobacco with resistance against this lesion former.

So, there are antifungal genes out there. We have a couple more we are working with, but we really need to investigate more of those, because you never know if any one gene is going to work against these problems in all the various crops.

There are mycotoxin detoxifying enzymes and genes that have been discovered out there. A few of our groups have completely elucidated the biosynthetic pathways of mycotoxin synthesis. It turns out that some of these pathways lead to inactivation of the toxins. They have the genes cloned for these inactivating enzymes.

It is tempting to think about transferring these into a crop, which would then enable the

crop to detoxify the mycotoxin. So, this is another approach that should be investigated.

Now, I mentioned insecticidal proteins. There is one called BT, which is a highly toxic insecticidal protein. That gene has been put in corn and what this shows is a corn ear, which has been damaged by an insect. Then right after that, the Fusarium moved in and infected the insect injury site.

Well, I don't have the result in front of me, but the BT-transformed corn reduces this insect injury and you get a drastic reduction in the amount of fumonisin that you get. So, that technology is already going on. It's in place. The problem is, there are a lot of insects involved that damage corn. The BT gene is only effective against certain members of the lepidoptera. There are all these other families out there that, we really need some type of defense against these insects as well. So, that work still needs to be done.

If we can get this type of information, then it offers the tempting possibility of being able to actually stack or pyramid antifungal and insecticidal genes, so that you can get the maximum control.

Here are some of the limitations I have to point out. Besides being very laborious and inefficient at this stage, until we can learn more about how to transform plants, many times it is cultivar [ph] specific. So, you can't necessarily transform your commercially viable plants. There is a lack of good gene constructs. We need to investigate better promoters, that is, a triggering mechanism that causes the gene to be expressed. We need better ones.

There are regulatory concerns that I have to point out and public perception. These are concerns that we need to deal with about genetic engineering approaches.

I'm going to end with talking about biological control.

Specifically, one problem we have with Fusarium moniliform, which makes fumonisins is, it has two phases in its life cycle. We can attack one phase, the pathogenic ear rot phase, because if we can control insects or if we can use disease resistance in the corn, then this might prevent this phase.

The problem is, there is an endophytic phase, which is symptomless, where the fungus is invading the internal parts of the seeds without causing any symptoms. However, recent discoveries have shown that, there is an endophytic bacterium that is associated with corn, that produces an inhibitor of this fungus in some cases. So, we need to learn more about what these endophytic bacteria are, learn how to exploit them and control practices.

Another form of biological control is to replace toxigenic strains with non-toxigenic strains in the field. This has been carried out by one research. This shows a formulation that contains a non-toxigenic strain of Aspergillus growing inside the wheat seed.

When the conditions are right in the field, this material will germinate and these non-toxic spores will out compete the toxin-producing strains in the field. This has been applied now for

three years in a row, 500-acre, large scale field plots. It shows very much hope that we can use this to control aflatoxin in Arizona cotton, grown cotton seed.

Just to summarize the biological control experiments that are going on right now, I just mentioned the Aspergillus flatus atoxigenic strain approach, which is a competitive exclusion strategy. I think this could also be used for some of the other fungi as well and develop non-toxigenic Fusarium, which could out compete the fungus in the field. This has really not been developed enough yet and think that there is a lot of room for future research there.

I mentioned the bacterium species that grows as an endophyte in corn. This could really be exploited in the future.

Last, but not least, there are epiphytes, that is, microbes that grow on the surface of the plant. For example, there is a yeast that was discovered on tree nuts, which apparently produces a toxin inhibitor, which could be useful in the tree nut area.

Finally, there are bacterial species that scientists are working with that we think could be applied to wheat or barley to biologically control the Fusarium graminearum.

So, in conclusion, I think the control of these various mycotoxin problems will be an integrated approach, a combination of several technologies. We need to gain a better understanding of the genetics and biochemistry of how these toxins are formed. How do the plants resist the attack by these fungi if natural resistance exists or the microbial populations and ecological factors that influence the levels of these fungi in the field.

Then, I think, with this information in hand, we can develop new crop varieties that are resistant and new biological control strategies and use these in an integrated approach to perhaps control this problem in the future.

That's my last slide.

DR. WAGNER: Thank you very much.

The next presentation is going to be given by Dr. Robin Huettel, from Cooperative State Research, Education, and Extension Service.

Robin is a national program leader in plant pathology, formerly worked in the plant diseases area for the APHIS organization, and she has been involved in working with the FDA on their guidance document for fruit and vegetable growers. She will talk about research needs emanating from that activity.

Guidance Document for Fruits and Vegetables:
Research Needs

DR. HUETTEL: Part of the initiative from the Food Safety Act was a partnership with FDA and USDA to develop guidance on good agricultural practices and good manufacturing practices for fresh fruit and vegetables. The outcome was a guide that has been developed over

the last year.

This guide has been developed in accordance to FDA's policy, set out in the "Federal Register" of February 27, 1998. The guide was developed with the appropriate public participation and scientific output. The guide document clearly states that, it does not establish legally enforceable rights or responsibilities and is not a legally binding document on the agency or the public.

These are solely guidelines that establish good agricultural practices to help growers, packers, processors and transporters of fresh fruit and vegetables, recognized sources of potential contamination by pathogens from field to transport.

In September of this year, FDA and USDA-ARS developed a multi-year research strategy under the Produce and Import Safety Initiative. Now, the purpose of this document was to provide a blueprint for detailed research plans in support of the Food Safety Initiative.

What I want to do today is, to discuss the guide to minimize microbial food safety hazards in fresh fruit and vegetables and discuss the research areas that were proposed in the FDA-USDA document, plus a few other research areas that could help either the grower, processor, packer or transporter of these commodities in utilizing these good agricultural practices, which are called GAPs.

In many cases, in order to practice GAPs, remediation may be needed to overcome the problems of the source of contamination. Even though the goal of the guide is focused on assisting the user and improving the safety of produce, alternative approaches must be developed so we can give these to the growers if they need them.

The research suggested in this presentation is to help to identify problems, while increasing our knowledge in the area of food safety, assessing risks and developing cost-effective interventions to prevent, control or eliminate microbial pathogens on fresh fruit, fresh produce. Now, one of the roles of CSREES is going to be in developing the education programs to delivering these GAPs and good agricultural management practices to the grower.

So, what I'd like to do now is, take you through this document and discuss some of these research areas. Now, some of this is going to be somewhat redundant with the first speaker, but I'm really pleased that I think we are on target with industry in recognizing the research needs.

Now, the purpose of this guide is to help industry by enhancing the safety of domestic and imported produce by looking at common areas of research need. The guide focuses on six areas that are associated with microbial risks from field through distribution. These broad categories are water, manure and municipal biosolids, worker health and hygiene, field and packing facility sanitation, transportation and trace back. The area that I will not discuss today is worker health and hygiene, as this does not fall under the mission of USDA.

The first and most important area, which you heard earlier, is that of water. Water is used

in crop production, in numerous field operations, including irrigation, pesticide and fertilizer applications, cooling and frost control. Post-harvest uses of water include rinsing, cooling, washing, waxing and transport. Water is a prime source of spreading localized contamination in the field, the facility or the transport environment.

Many of the organisms transferred by water have been discussed today, but it is not currently known what levels of contamination in water can be a problem.

The guide states that, whenever water comes in contact with fresh produce, the quality dictates its potential for pathogen contamination. The guide also states that, the quality of water in direct contact with the edible portion of the produce may need to be a better quality than the water in which the edible portion of the plant is minimal.

The quality and sources of agricultural water vary considerably. Surface water may be more contaminated in areas where runoff is affected by animal operation. While water, rivers, streams and irrigation ditches are all subject to contamination, therefore, the guide recognizes that sources and distribution of water use are important in GAPs and the user must be aware of the relative potential as a source of contamination.

Growers, as stated earlier, really have sometimes little control over the factors that affect watershed. Right now, microbial testing may be of limited usefulness at this time. However, developing sampling methodology to determine levels of contamination, especially low level microbial contamination, might assist growers in determining the risk of the water being used.

It is also important to refine, improve, and determine applicability and validity of laboratory methods for recovery, identification and enumeration of microbial pathogens. This research needs to be conducted under field conditions to determine the survivability of pathogens in soil and also in water.

Another source of water delivery, as discussed earlier, is through irrigation. Irrigation, there are many different types. There are overheads, center pivot and drip through. Generally, however, the type of irrigation system used reflects the soil type, the crops, the growing condition and the water availability and restriction of that region. Questions have been raised on whether the various types of irrigation systems--which type of irrigation system might be less likely to introduce contaminated water on to the edible portion of the produce.

Research needs to be conducted on the various systems and the survival of pathogens. Investigation of the macro- and micro-environments that the microbes inhabit, including the biofilm formation of pathogen attachment under different water regimes should be conducted. Consideration must be made as to where to sample, distance between introduction of water into an irrigation system and its exit points and whether standing water remaining in a system is of importance and whether pathogens can increase under these conditions.

Another area of importance in preharvest production techniques might include breeding of

resistant cultivars, not just to reduce pathogens, but to change the surface conditions which might reduce the adherence of these pathogens to the outside of the plant.

Other areas are discussed in this guideline, too, that are of importance to the growers. One of these is to make the grower aware of existing practices and conditions and potential sources of a contamination, such as, malfunctioning septic systems or on site contamination from animal wastes. Also, knowledge of current and historical land use can determine possible sources of contamination.

As water is often a shared resource and runoff of manure from other farms, contamination from feedlots upstream and just the topography of the land can lend itself to contamination. In order to determine levels, again, sampling methodology for pathogens in well water, runoff, irrigation ditches need to be developed. The use of soil and water conservation systems that might protect water sources, such as, grasses, diversion berms and other methodology should be investigated. There is little understanding of the competitive, antagonistic and symbiotic interactions between pathogens and the natural microflora on produce. Ecological studies should be conducted in this area to help to understand the soil and plant microflora.

The second major source of agricultural use is processing water. The guide states that processing water should be such a quality that it does not contaminate the produce. Water used during post-harvest handling of fruit and vegetables often involves a high degree of water to produce contact. Even though the water can remove pathogens, it may also serve as a source of cross-contamination.

It is important to follow good manufacturing practices to minimize contamination of processing water. Of course, there are regulations on FDA and EPA on types of water treatment, but these must continue to be developed. Research in this area should also be conducted on novel physical, chemical and biological treatments for reducing contamination.

Other research areas involve investigating the efficacy of rinse and wash procedures in reducing pathogens, including surface treatments that are non-chemical in nature. Many types of produce are water-sensitive and cannot or are not treated. Alternative methods for this produce need to be developed.

Other types of research that would minimize contamination of processing water include determining how bacterial stress responds to stimuli, such as, heat, cold, Ph, disinfections and the use of oxygen reduction potential in treatment water.

The next major area recognized in the guide is the consideration of manure and municipal biosolids. As stated earlier, treated manure and biosolids are effective and safe fertilizers. Untreated and improperly treated manure or biosolids obviously can enter surface or ground water through runoff and contain pathogens that in turn contaminate the produce. Growers need to be alerted to these microbial hazards in fecal matter that may be unwittingly introduced into the

produce, growing and handling environment.

Good agricultural practices for the use of animal manure or biosolids into treatment to reduce pathogens and maximizing the time between application to produce areas and the harvest of crops is important. This is stated in the document.

As discussed, there are various treatments available for raw manures and composting. However, research is needed to determine which treatments are most reliable, predictable and consistent in reducing or eliminating these pathogens.

Recontamination can be a problem. So, research should also consider mechanisms to prevent recontamination of properly composted manure. Untreated manures need to be managed through soil incorporation, with significant sufficient time between application and plant.

Research is needed to determine the safest soil application technologies, such as, broadcast or in furrow, seasonal introductions, and things like that. Manure storage and treatment sites should be situated as far as practical from fresh production and handling areas. Barriers or physical containment to secure manure storage is needed to prevent runoff, leaching and wind spread. Research is needed to determine pathogen survival and dissemination in all manure sources.

Municipal biosolids are also recognized as beneficial as soil amendments. Requirements for their use are set out in Title 40 of the Code of the Federal Regulations and require either elimination of pathogens or significant reduction of pathogens, along with other restrictions. Research in this area needs to be similar to those that I discussed for the use of manure.

The last part of the section on manure and biosolids is, a consideration of animal feces as a source of contamination. It is recommended that growers prevent entry of domestic animals into fresh produce fields, vineyards and orchards during the growing season. Growers should determine whether the surrounding fields and farms may be a source of contamination. Research is needed to develop soil and water conservation techniques that reduce this type of contamination.

In areas where wildlife concentrations are high, growers should establish these GAPs to deter or redirect wildlife away from growing areas. Conservation practice to deter these high populations of deer or those of water fowl must be developed.

Then another area of research that was discussed is the reduction in pathogens in animal feces by looking at parasite carriage and shedding by farm animals.

The next area in the guidelines that I will discuss is looking at field and packing house sanitation.

Under field conditions, soil, fertilizer, workers and harvesting equipment can also be a source of pathogens. Therefore, cleaning and maintenance of equipment is very important in reducing contamination. The maintenance of building fixtures and other physical facilities and just

keeping the grounds in good condition can also help to reduce contamination.

Research areas that need to be considered are, appropriate pest control methodologies that might prevent contamination by insects or rodents. Research is also needed to improve packing containers and packing methods that may either introduce pathogens under field conditions or bring them into the packing facility.

Survivability of microbials is a concern due to resistant strains which are known to occur. Research is needed to define the physiological or genetic mechanisms that microbes utilize to become resistant to traditional food safety barriers such as heat, cold, pH. Also, research needs to be looked at to understand the development, amplification and maintenance of resistance by these organisms under stress conditions.

Transportation is also recognized within this document and certainly the proper transportation of fresh produce from farm to market can help in reducing potential contamination. Research is needed on temperature control or post-harvest storage techniques that might minimize microbial contamination, such as, controlled atmospheres and various types of temperature control.

Now, the last section of the guide is on traceback. Traceback is the ability to track the food back to the source, to their source. Now, this is a very important area that can be managed by the grower being able to track where the produce, his produce goes, which packing house it goes to and then to market. Often times, produce is all collected together and there is no traceback if there is an outbreak at a different source.

One area of research that can be very valuable with this is, the development of molecular market techniques to identify particular pathogens, to facilitate this traceback.

In conclusion, the outcomes from the research described in this presentation will assure that good agricultural practices can be utilized by the grower, processor and packer. Further, this research should provide reasonable and cost-effective alternatives or solutions to keep our producers competitive, while protecting our fresh fruit and vegetables from microbial contamination.

Thank you.

DR. WAGNER: The last speaker for this session is Dr. Mark McLellan, who is from the Cornell Institute of Food Science, at the Geneva Station, who will talk about fruits, vegetables and fluid commodities.

Mark.

Fruits, Vegetables, Fluid Commodities

DR. MC LELLAN:

I have no slides, so if you could bring the lights in the house up, I would appreciate that.

Thank you for the opportunity to talk about research needs in the fruit and vegetable

industry. We think in terms of a farm-to-fork issue in this, certainly one that, from the point of view of fruits and vegetables, this is not something we want to segregate as a discussion item from animals. It is an intertwined issue and there are many confounding connections between our animal husbandry, our wildlife management and our farming practices that do need to be addressed.

One of the issues that you will find us talk about often is, the need for common sense answers, rooted in a sound science. We have had many examples where we might not have necessarily gotten off on the right step in that direction. I would like to point us in this discussion to four areas that research priorities really should be set to and focused on, three specific and very common ones and, the fourth one, probably not as common.

The first is prevention on farm. We will come back to that one in detail. The second is looking at our processing system and handling systems in processing plants. The third is in the retail handling and food service area. The fourth outside of the three of these is, more an opportunity to look at how we do our regulatory process and generation of policy as it applies to food safety.

In terms of our prevention of cross-contamination and pathogens on the farm, as I have heard a number of speakers already talk about, the good agricultural practices or GAP, you might think in terms of our current needs is trying to find out what the gaps in GAPs are. It really begs the question.

If you walk into a program where farmers are attending and ask them what does good agricultural practices mean to them, let me assure you, they do not think of it in terms of the view we think of it. They think of it in terms of how much crop they get out the door at the end of the year and how much they put into getting that crop out. That is good agricultural practices to them.

We have not yet even begun our educational process. Robin, I think, we have our hands full there. Clearly, there are gaps in our knowledge here in terms of how we will apply good agricultural practices and call for it. There are serious areas of research, farm operation assessment.

How do you take a farmer and instruct them, educate them and build an assessment process of what are the issues involving food safety associated with that farm?

Documentation of standard operating procedures, elucidating, just getting those standard operating procedures elucidated and documented is really a struggle when you sit down and talk to some farmers. To have them look from soil on through to output, your product, is a challenge, too. Many times they think of just from harvest on and you really have to encourage them to start at the very beginning.

Having them also have a very, very keen awareness of chemical, microbial and physical

hazards; the question is, are we ready to go into GAP? No, not at all. We have not yet begun to instruct farmers that they are the first step in terms of a safe food product. In some ways, they should be considered the most critical step and it is going to be a serious challenge for us to walk into applying good agricultural practices and institutionalizing them in terms of our production environment.

Previous speakers have talked about water and I am not going to go into that in detail. I certain could not add too much to the discussion of manure. However, I would be remiss if I don't spend a few minutes, because if there is one issue in terms of our agricultural practices and the hazards of contamination, I think you have to turn to manure.

Whether it is coming in as a secondary contamination in water systems, it tends to still point back to manure issues. Quite frankly, we have not done a good job in terms of tackling how do you stockpile. How do you treat? How do you handle; how do you manage manure?

A classic example is a grower who came to us last year, a very large grower with a dairy herd operation on one side of his operation and a very effective, very profitable vegetable growing operation on the other half. Of course, he was looking at merging the two and using the agricultural input across the entire spectrum there to have a very efficient process, a wonderful, wonderful concept.

Yet, the very simple question of, Mark, how do I know what to do with my liquid manure in terms of applying on a side dressing, do I use a three-inch furrow or an eight-inch furrow. What is the difference? How will it effect the quality and cross-contamination on my vegetables? We have no answers really to point to, no good body of work that is going to support him in that area.

So, we think there is a lot of room for focus here. Believe me, we understand even as food scientists, the incredible value of manure and soil management. We simply cannot afford to lose topsoil at the rate we are and we do have to look at this very important input in our agricultural system, something we need to protect and work into the system.

It does beg questions concerning organic practices. We do have to be careful about educating the proper way to approach use of these systems. That is something to keep in mind.

It also brings to beg the question of domestic versus imported food supplies. There is a very big area here in terms of research. How do we take this global food supply and create a level playing field, a level growing field? Is it inspection? No, of course not. Inspection simply helps us sleep tonight.

Really what we need to do is build in ways to be delivering a safety assurance system on a global basis. That is going to be very challenging for us.

Raising safety awareness, bringing import and domestic food production to equivalent levels of safety, implementing HACCP where possible. Challenging? You bet and there is going

to have to be research. How do you teach this and how do you encourage this? What are the economic benefits to doing this and how do you build in the kinds of systems that are going to encourage this?

It must be done if we are going to reflect on the fact that we truly are in a global food supply.

Let me move to the second category of processing and handling of food systems. With my own experience being more to the juice side, you will see some of my comments lean that way.

Clearly, the thing that we most predominantly lean on in terms of process system is, it is not HACCP. HACCP is well on its way and it is coming in very strong now. What we have truly leaned on tremendously has been good manufacturing practices, good manufacturing practices. Yet, there are still very large numbers of segments of our processing industries that don't even have that and a classic example of that happened in the last few years, which was the juice industry, the fresh juice industry.

There was absolutely zero recognition, for the most part, of good manufacturing practices. Clearly, this is a case where, if we took a step by step approach, their first step should have been to go to the development of good manufacturing practices and then to move on from there. We will come back to that topic in a minute.

If you look at it from the manufacturing point of view, you can walk through a number of unit operations, starting with harvesting, methods of harvest and even your rules for procurement, sorting, cleaning, and something as simple as a brush washer. Have you ever thought about what a brush washer is, how it operates and how do you quantify its effect on food safety? It does have a quantifiable effect. Surely, we can all agree to that.

If you take this product, whether it be a cherry, an apple, a plum, whatever it might be and you assume that there is a microbial load to that. Now, you are going to apply it or send it through a unit operation called a brush washer. There are a lot of issues that we don't naturally think of in terms of assessing what the impact for the safety is on that unit operation.

In fact, that is exactly where we have to get to. We have to get to the point where we can look at each unit operation and be able to understand and have a mechanism in place that we can assess its impact. For a brush washer you might be talking about orientation of the fruit, the bristle type, bristle density, speed, orientation of that rotational speed on the bristle system, duration through that brush washer, whether it is done in a dry system, done with a hot water spray, cold water spray, et cetera, et cetera, et cetera.

The point is, as you look through typical unit operations, we are just now beginning to think in terms of each of them playing a critical role in assuring the safety of our product and, in fact, that must be there.

Later on, you are going to be hearing more about processing steps, things such as thermal processing, physical and using any range of the electromagnetic spectrum. So, I am not going to get into that detail.

Again, it brings us to the idea that, as you are looking at a manufacturing process, each and every unit operation has to be looked at in terms of its potential, in terms of contributing to food safety, a little bit of a newer view that our processors have not been familiar with.

One caution is in the area of minimal processing. We are very encouraging of a fresh food supply. We all want a fresh fruit and vegetable food supply. In our rush to do that, we would like to consider minimal process techniques that keep that freshness and, yet, deliver that extended shelf life. Of course, the question is, what do you set up in terms of the ecology of those systems? What do you set up in terms of a non-competitive ecology that might allow for a pathogen outgrowth where in a natural environment, where spoilage organisms are still present?

You would not get there without seeing significant spoilage and, therefore, not using the fruit or vegetable. So, there are some interesting research issues there.

Let me now bring you to the third area and although it may not be quite the area that this group is focused on, we darn well better keep in mind that it is one of the most critical areas. Nancy mentioned this and this is in the retail area, the food service area.

All of what we do to insure the safety of the raw material, of an ingredient, of a fruit and vegetable, up to that point, can just go right out the window if it is not handled well. Whether it be in procurement, not only looking at quality, but looking at safety issues in your procurement process, storage and cross contamination--and everybody has their stories.

Literally, two weeks ago, I sat with a public health inspector from New York state and he told a very similar story, Nancy, where he was in actually to congratulate a restaurant for their exceptional design, layout and operation. He was in the kitchen with the chef, with the owner. They were standing around a table and in walks a worker, opens up the walk-in refrigerator, grabs the tray of chicken and lifts it up over the salad. Of course, it trickles all through the salad. They all just looked at it and said, well, so much for that. They yanked all that material out.

It just goes to show you. I mean, even from the point of view of an excellent operation, human error can bring you to a catastrophic condition. In the retail handling, food service area, that is very important.

Let me bring you now to the fourth area, policy development, improving policy development and looking at how we generate rules, regulations and policies.

I think it is time that we take a look at the mechanisms that we have in place for doing that. The answer may well not be, take a bunch of specialists, throw them in the back room and have them devise a rule or policy. Throw that out and let's see if the hearing process throws enough darts out to kill it. That might not be the very best common sense approach.

I think there is room there to expect that regulations should come out based in science, not with the cart before the horse, but rather based in science, with sound numbers and information behind the rules and regulations, with alternatives that make sense. You can look at a number of different places where this has come up an issue. As you might guess, you might talk about certain rules and regulations that talk about implementing HACCP without even the idea of a target organism, let alone a test organism and many, many other unknowns. You can go on and on.

I just think that this is a good time to take a look at how we generate our rules and regulations and think through to a common process, a common-based system that is based really in science.

Thank you.

Discussion of Papers

DR. WAGNER: Before we open this up for questions, I want to just bring up a collateral issue. That is that, tomorrow, beginning at 10:30, we have a public comment period which will run for the balance of the program tomorrow, on Friday. We have had a few people who have asked about being added to the list.

If you are interested in giving public comment tomorrow and have not already signed in, we will try to accommodate you at the end of the program, in the afternoon.

Dr. Jennifer Kuzma has been keeping track of names. Jennifer is back there by the projector. So, if you are not on the list and want to be added, please talk to her at that time.

Once again, for those of you who weren't here at the very beginning, the reception this evening will start at 5:30, being sponsored by the Alliance for Food Safety. It will start at 5:30 in the adjacent room, the Washington Room, right next to where we are now.

I would now open this up for a discussion of the presentations which we have just heard. Are there questions from the floor?

Yes?

QUESTION: There has been a common theme throughout most of the speakers that, manure is a major source of pathogens in food safety. You've talked about composting, but I haven't heard anyone discuss the benefits of anaerobic digestion, which eliminates the contamination or cross-contamination for some of the processors.

DR. WAGNER: Could you identify yourself, please, for the record?

MS. SORENSON: Ann Sorenson, from Utah State University.

DR. WAGNER: Thank you.

Who would like to take that?

DR. HUETTEL: Well, I think any area like this, there is certainly something to be

included. We did not go into detail with all the various types of approaches, to looking at manures and compost. Certainly, that is one that needs to be considered.

DR. WAGNER: Other questions?

Yes, Caroline.

MS. DE WAAL: Thank you, Caroline Smith DeWaal, with the Center for Science in the Public Interest.

Robin, my question is for you. In designing the GAPs document, was thought given or was research done on the language in that document that could have been used to best communicate to the grower community? I was struck that the language in the document is vague and confusing. If I were a farmer in Vermont where I grew up, I may not understand all the messages that were coming out. So, was any research done on the kind of language used in the document?

DR. HUETTEL: I think that the document was developed in general to be somewhat vague because there is no research in many of these areas. These are really just principles, areas of recognition to be able to make the grower aware these things might exist there, and there were many public meetings. There was input from many groups that were incorporated into this, however.

MS. DE WAAL: Can I just have a followup?

I went back and looked at our comments on the original document and one of our comments, one of our major comments on the original proposed document was that the language was not clear. In the document, you talk about having this vague and unclear language put into many different languages so that it can be used by our foreign trading partners. I just question the value of the current document being translated into lots of different languages.

The fact that water is of different quality means something very different in this country than in a third world country. So, I wonder if there is any thought to perhaps putting it in language that is clearer and more direct?

DR. HUETTEL: What I would have to do is, defer to someone from FDA. USDA had a support role in reviewing the document, but it was written by FDA. I don't believe there is anyone here to address those comments.

DR. WAGNER: I might just add though, Caroline, that our agency, CSREES, has been charged with developing, having a major role in developing the educational program. We hope that in doing that, we will be involving the grower organizations and the land grant system to develop the educational materials much in the way that Nancy Nagle and Mark McLellan have also talked about--will speak to some of those questions I think you are raising.

Other questions?

Yes.

Dr. Maher: My name is Ted Maher with CSREES and I have listened attentively. I'm a little off my turf when it comes to the technology and the technical subject matter. My question really relates to an extension technology transfer-type question and it is for anybody on the panel.

Listening to the examples of research needs relating to water and waste water and municipal biosolids and so forth gives rise to a couple of questions. I hope this is not impertinent in a group of researchers from universities and federal laboratories.

The first question is, to what extent do we ensure that the research we identify, the research needs that we identify are, in fact, research needs rather than the facts that these things might already exist somewhere, that the research has already been done and that the technology exists somewhere? How do we insure against that?

The second question is, to what extent do we, when we identify research needs, also look outside of the traditional research envelope and the traditional channels for research and look to other agencies of government or other sources of research that may have already been performed? Maybe the classic example is HACCP, which is a NASA technology, developed in the mid-'60s for the astronaut core. To what extent do we consider the possibility of spinoff or technology transfer from other sources?

DR. HUETTEL: Well, generally, when you have a new research initiative, you bring in the subject matter experts from various agencies. The research that has been identified here is through USDA, Agriculture Research Service, through the land grant system and also input from industry.

Generally, these are the scientists who are most aware of all the areas. These are not only in the preharvest area, plant pathologists, food microbiologists. So, I think that probably a very good job in assessment of research is done. As a matter of fact, Cooperative State Research Service, when the food initiative was first announced, did a very extensive research on all the projects and all the dollars associated with these research projects that were being conducted in the USDA.

So, I think that there is a pretty good feeling that, most of the current knowledge has been recognized and documented at this time.

DR. WAGNER: Dr. McLellan.

DR. McLELLAN: One of the exceptional ways, of course, this happens is by running a competitive grants program, where you have a panel of experts, outside experts that review these, a panel that discusses it in-depth before any funding decision is made. It is one way to insure that you have the broadest review, to make sure that the work is original is a fact and is appropriate for the problem at hand.

DR. WAGNER: Anyone else want to take a shot at this?

DR. WAGNER: No? Okay, other questions?

Yes, in the back?

DR. BuLLERMAN: I'm Dwight Bullerman, from the University of Nebraska. I'd like to comment on Dr. Cleveland's talk, just make a couple of points.

I agree that, while plant breeding and biological controls, genetic engineering may ultimately lead to prevention of mycotoxin contamination of cereal grains, for example, the fact is, contamination is occurring now. Fumonisins, for example, can be found in food grade corn. Corn is going into human food products and low levels of fumonisins can be found in a number of processed, corn-based foods.

We don't really know the effects of low levels of exposure to low levels of these toxins over time. For example, the Fusarium toxins have immunosuppressive and disruptive properties that can be immunosuppressant and, in some cases, even immunostimulation can occur. We don't really know what the effects are in terms of long term exposure in healthy individuals as well as individuals who already may be immunocompromised as a result of either age or other disease.

The other point I would like to make is that, food processing systems do have an effect on the amount of these toxins that are found in finished products. For example, milling of corn removes fumonisins from certain parts of the kernel that concentrate in the germ and bran fraction. Whereas, the grit fraction that is used to make snack products and breakfast cereals remains relatively free of fumonisins. So, there is some evidence that certain foods are free of these things as a result of processing.

High temperature processing, extrusion, roasting also can reduce the levels of these toxins in finished products. So, I think there are some other areas of research that are also important.

DR. CLEVELAND: As far as the effects, long term effects on humans, that, of course, is not in my area. I do know that there is a large study going on, on the toxicological aspects of fumonisin, whether or not it is a carcinogen or not.

Dr. Robens is here. She is with our program staff. She knows a lot about that study. I think FDA is spearheading it and there should be some useful data there about what is the risk to humans, I think, coming out of that study.

I just want to point out that, in no way am I saying we should reduce research on the processing-type area as well. I'm just saying that, I think in the long term scheme of things, we need to try to prevent it before it ever gets into the food supply. If it gets in there, I'm not sure you can ever be certain that you have completely removed the problem. As far as that goes, I can think of specific examples where the product might be degraded in some way and it seems by appearances to be safe at that point, but then the degradation of products might be dangerous as well.

However, I agree with you that, sometimes you can partition these toxins out and get rid of them out of a certain component. Don't get me wrong. I'm not trying to say that research in

those areas should be reduced. I'm saying that some of these other areas should be enhanced. That's my point.

DR. WAGNER: Other questions.

DR. DRAWN: I'm Ann Draughton from the University of Tennessee, at Knoxville. I have a question for Nancy Nagle.

I realize that we need to get our own house in order as far as produce in this country, but we haven't really talked much about imported produce and we use a lot of that.

Has United Fruits and Vegetables taken a position on the equivalency standards for fruits and vegetables similar to what we have for meats and poultry in existence already?

DR. NAGLE: Well, unfortunately I really can't speak totally on what United's position is on the equivalency standard. I would be happy to get you information on that.

We do feel that there needs to be significant attention, again, internally. We have to know what we are doing in this country, so that we can set appropriate standards. I'm aware that United has a feeling and there has been some talk about judging an entire country. We feel very strongly that, that is an inappropriate response; that there can be operations within a country, within an area or region that can be outstanding operations and vice-versa.

We know that there are U. S. companies that have gone into a number of these countries and gone in and built water treatment facilities and whole infrastructures around that. So, to just say that, country x does not have the water treatment infrastructure, et cetera that we have in this country so, therefore, produce can't come in from there, we don't agree with that.

It has to be, what do we want to say, on a ranch by ranch, farm by farm area in certain cases, because if you have built a water treatment facility, you may have better water than 90 percent of the stuff in the United States. So, we don't believe you should go in and summarily say, no produce from Guatemala or some country like that.

DR. WAGNER: Okay, other questions?

Yes?

MR. KNABEL: Steve Knabel from Penn State.

One of the thoughts I had is that, there seems to be a lot of research in specific areas, in the area of microbial ecology, such as, looking at humans' and animals' manure, various environments, various foods and then also in the human. I'm just wondering if it would be a good idea to take a more holistic approach and have vet microbiologists working with food microbiologists working with environmental microbiologists, so we can understand the whole microbial ecology of these pathogens and how they successfully navigate all these different stages in order to cause infections to humans.

Maybe I'll just throw that out to the panel, what do they think of that possibility.

DR. CLEVELAND: Hear, hear.

DR. HUETTEL: Yes.

DR. WAGNER: I think we are trying to move more in that direction. There are some projects that are now in progress, for example, with the Salmonella 104 strain, there are some projects that are looking at the whole issue of how that organism moves around within, say, a dairy farm, between people and animals and the environment. We are trying to move in that direction.

These studies, of course, become much more expensive than the more segmented kinds of actions.

Other questions?

[No response]

DR. WAGNER: If there are none, I would ask you to join me in applauding the panel. We are actually ahead of time.

[Recess.]

SESSION IV Moderator: Dr. Richard Ellis [3:32 p.m.]

DR. ELLIS: I'm enlightened by some of the foresight that our founding fathers had when they called us to provide for the general welfare in the Preamble of our Constitution. I guess I have a sense of optimism just by the response and turnout at these types of meetings that, we certainly are moving in the right direction in terms of providing for and improving the nation's food supply.

As a way of introducing this session, I would like to just use a very small story.

A few months ago, one of the national program staff decided to bring two people in to handle the food safety research. So, I sort of kiddingly asked the new member, do you deal with the live animals or the dead animals. He said, I deal with the dead animals, the post-harvest. Unfortunately, many of the things we are concerned with, don't die when the animals does.

So, we are here to address a different perspective with post-harvest and identification and control of pathogens in foods.

We have four speakers this afternoon who represent not only industry but academia. Our first speaker is Dr. B. K. Girdhar. He has a Ph.D. in food science, from Ohio State University. He is currently head of research and technology for OSI Industries, which is a multinational food processing company, headquartered near Chicago.

Our second speaker is Dr. Mike Doyle, who has a background in bacteriology and a Masters and Ph.D. in food and microbiology, from the University of Wisconsin. He is currently Regent Professor of food and microbiology at the University of Georgia and the Director for the Center for Food Safety and Quality Enhancement.

Our third speaker is Dr. Elsa Murano. She has a Ph.D. also in food science, from Virginia

Tech, under Merle Pierson, who will talk to you tomorrow. She currently is Director of the Center for Food Safety and the Division of Animal Science, with Texas A&M University.

Now, the fourth speaker is Dr. Michael Davidson. He also has a Ph.D. in food science from Washington State University. He is currently Professor of food and microbiology, in the Division of Food Science, at Washington State University.

I am not going to go through and give you a lot more details on the individuals, other than to say that they have the right pedigree or they would not be on the agenda today and largely because of their research activities as well as their publications. So, with no further ado, I'd like to introduce first speaker, Dr. Girdhar.

Processing Industry

DR. GIRDHAR: Thank you.

Good afternoon, everybody.

I would like to thank the organizers of this conference for inviting me here today. I hope the food processing industry stays involved with this Alliance for Food Safety. After all is said and done, after all the presentations have been made, the research taken care of, it is the processing industry which is going to implement the results of all this research and deliver us safe food to the common public. So, thanks, again.

The topic of my presentation is the research needs for the detection, prevention and risk assessment of food-borne pathogens in the beef processing industry. Before I begin, I have to give full credit for this presentation to the Beef Industry Food Safety Council, of which I am a full-time member. I did spot a couple of other members here today. We have been meeting for almost 18 months now. We have met five or six times, either through conferences or we have phone calls. We have developed a very good agenda for the research.

Most of what I am going to present pertains to 0157, but as we all understand as we go through it, very easily, it could pertain to others, like Salmonella or other pathogens. I will focus on the beef industry, because OSI, although it is a multinational food processing company, beef is our number one food product. We also handle pork, chick, turkey, vegetables and fruits. It is all processed.

Very briefly, the Beef Industry Food Safety Council, we call it BIFSCO, is composed of producers, packers, processors and researchers from academia, industry and government. It was formed in October of 1997 to develop industry-wide, science-based strategies to solve the problem of E. coli 0157:H7 and other food borne pathogens in beef. To accomplish this goal, members of the council were organized into five working groups, I would say, the most important being research and science, which I am a member of. The other being consumer education, let me focus on that a little bit.

I think communication is a major issue here, because I have heard several speakers today

and I also say it is common sense which takes care of most of the problems. HACCP is great. All the research is great. Technology is fantastic, but it is the GMPs. I think it is very easy and it does not cost too much money to implement some very minor, common sense things which can eliminate at least 80 percent of the problems, not only in the beginning, not at the farm level, also at the processing floor, but also at the customer level, especially in the food service industry. I will talk about that a little later.

The research science working group initiated a process, to develop a comprehensive research agenda, identifying key researchable issues necessary to resolve the E. coli 0157:H7 issue for the beef industry. This agenda evolved from an extensive review of existing literature and ongoing research, coupled with practical industry experiences. It is based on needs or problems that must be resolved.

We had very lively discussions. I forget the name of the lady who asked the question, if the research already exists. Maybe you can always miss something, but that was part of our goal, that we wanted to research all the databases, all the universities, government research literature, private industry, to make sure that we don't waste time and money on something which already exists.

What we did was, we divided the research needs into four segments. I will list each segment. I have listed each segment here and I have given three or four top priorities in each segment. After that, we all got together and we voted. We had a list of these and then some. We had a list of about 20 to 25 research topics and we were all asked to vote from one to five. After those votes were in, we picked the top five.

After I go through all these, I will present the top five priorities that we feel are necessary.

The first segment would be the preharvest research, gaining a better understanding of the host-pathogen relationship to aid in the identification of potential preharvest critical points and intervention strategies. I know there is a lot of data which exists and I know there are a lot of papers being published and I have attended quite a few conferences and I have listened. I think there is still a need to put it all together, be it by research or be it by literature search.

Identify production and management practices that influence growth, shedding and spread of E. coli 0157:H7. Also, gain a better understanding of the ecology of E. coli 0157:H7.

The next segment would be beef carcass conversion. Develop a system of microbiological verification of the slaughter process for beef. That is not to say that the microbial verification is the answer. One negative sample does not mean that it is all clean. If you consistently keep getting positive samples from one supplier or one ranch, then you know there is a problem.

Demonstration project of the microbial advantages of utilizing multiple new intervention technologies in the slaughter process. It could be hot water washes, steam vacuum, steam pasteurization, microbial acid washes, anti-microbial acid washes.

Develop benchmarking data on microbial profiles, potential recontamination of product during the carcass conversion process.

At OSI, we participated in a study, steam pasteurization. I will not name the sources where we were getting our supplies and we had a six-month study. At the end of the study, there was no difference. We could not build a statistically significant difference the steam pasteurized versus none. Then we started investigating. There has to be a reason for this.

We found out that, although the product was being steam pasteurized, after that, it was being put on the same floor, same tables, same knives, same people, same storage, same transportation. It was being recontaminated. I mean, common sense is very simple.

Ground beef processing: the first one is, develop sampling and testing protocol and recommend microbiological testing as an integral verification step of all processing leading to the manufacture of ground beef. Only a verification; a negative does not mean it is good, but if you have consistent positives, you know there is a problem there.

Develop a protocol for testing forE. coli that facilitates the definition of lot sizes. There is a lot of confusion out there.

Develop irradiation guidelines for ground beef products. I will talk about that a little later. There is a lot of talk about that.

The microbiological enumeration of pathogenic microbial loads in ground beef. You know, right now, we say either it is positive or it is negative. But what is the amount?

Research new microbial intervention system for ground beef and cooking systems for beef patties. That goes for the processing floor and also to the end user, especially the food service establishments, cooking the patties.

Retail food service: determine the microbiological profiles for beef raw materials and finished ground beef product from production to retail, a verification of hazard.

Development of a common strategy and tool of management that provides a uniform system of assessment and administration of food safety management at retail and food service establishments, make it uniform.

The criteria for voting on the top five needs were: 1. What is the magnitude of the problem and what benefit is it's solution to the industry? 2. Does it need to be solved regardless of the required dollars, no matter what it takes. 3. What is the probability of success in resolving an issue in both short and long term, if a specific research effort is initiated. 4. If successful, what is the probability of rapid industry adaptation to truly impact beef safety. Research is good, but it has to have a practical application.

Considering the total national research agenda, in what areas are the current research efforts concentrated relative to the critical voids in our knowledge. Also, has adequate funding been committed to specific research areas by other agencies? If so, we don't worry about it. If

somebody else is doing it, let them do it.

This is what we thought was necessary, the top five priorities. The first one in the preharvest segment is to gain a better understanding of the host pathogen relationship, to aid in the identification of potential preharvest, critical control points and intervention strategies. I know it has been talked about this morning here.

Identify production and management practices in the feedlots that influence growth, shedding and spread of E. coli. Develop sampling and testing protocol and recommend to the industry that microbiological testing is integral for verification of processes steps, before grinding of trim into ground beef.

It is not a complete solution, but I will repeat one more time. It is a verification of HACCP and other GMPs and cleanliness.

Develop irradiation guidelines for ground beef products. Then finally, gain a better understanding of the biology and ecology of 0157:H7.

This kind of explains those goals, our research needs on the host-pathogen relationship. Establish, define protocols and procedures for measuring their prevalence. Where data are lacking or inconclusive, identify the problems of 0157:H7 in segments of the beef production sector, farm branch, background and feedlot, et cetera.

Determine the reservoirs for E. coli, such as, birds, rodents, other wildlife, bird droppings. We talked about that today, this morning. Improve the knowledge of the epidemiology of 0157 in cattle, how it spreads, colonizes cattle, levels of exposure and time required for colonization and cleaning out the organism.

I'm going to go a little faster. I think I'm running out of time.

Identify production and management practices that influence growth, shedding and spread. Determine the level of contamination on hides and hair of cattle at slaughter plants and factors that affect level of contamination. Investigate management variables, such as, diet ingredients, feed and water additives, growth promotants, time on feed, health management practices and health status, stress and handling, production facilities, management practices and feed withdrawal.

Understand the effect of modern production practices on the diversity and properties ofE. coli, population and the emergence of new food-borne pathogens, which might be related.

Then again, on number three here, we need to do it to evaluate the microbiological quality of the product all along the processing chain, from beginning to end. We talk about HACCP. Are people really following that? Are they really doing the GMPs or not? Are they keeping the place clean or not?

Also, to implement that, we need to develop some real or near real time tests, that don't cost $200 a test, something which is quick and something which is economical so that people can

do it. If it is going to cost me $200 and 24 hours to do a test, I might skip a few.

Also the sampling size and strategies should be meaningful for pathogen detection at the present. We get trim in 40,000 pound loads. If I check 25 grams, I don't know how much sense it makes.

The first meeting we had, this was quite hot at that time and the USDA later approved that. We are still waiting for the guidelines. All the work that I have done and my company has done and all the research data, I think there is a big need for somebody to really take this project and tell the people. Tell the processing industry what the levels are, what the maximum ratios are, what the packaging material is, what the shelf life is, what the effects of irradiation on the sensory qualities of the product are.

So, there are lots and lots of questions and so far, very few answers. So, it is quite important. The guidelines will be coming shortly, but I think it is many, many years away before you see pound one irradiated, because nothing exists. We don't even have the packaging material right now, which was approved and which works.

The last one, I had gained a better understanding of the biology and ecology of 0157. Determine the effects of human variables, such as, pH, fatty acid. Establish and understand the mechanics of colonization. Understand the interaction with other microflora. Determine how 0157 acquires acid tolerance and then conduct a detailed genetic characterization of 0157. Implement applied intervention research based on knowledge of the basic biological properties obtained from the preceding research efforts.

In conclusion, I must say, let's find simple solutions. I think 80 percent of the problems can be solved by not spending a lot of money, but by using common sense. So, let's all communicate.

Tell the kids who are working in the restaurants to use GMPs. I could make the best hamburger patty. I could irradiate it and I could package it in a $5 package, but if this person does not clean his or her hands after using the washroom and serves this hamburger, what good is it?

So, somehow, we have to communicate that at all levels, GMPs, common sense, HACCPs.

Thank you.

DR. ELLIS: Thank you very much.

Our second presentation this afternoon is by Professor Mike Doyle. I don't think he needs much more introduction.

Improved Detection Methods

DR. DOYLE: Thank you, Dick. I appreciate that introduction.

I have given a lot of talks in the past, but you're going to hear a first. A few weeks ago, I

received a call from the personnel at the American Society for Microbiology. They asked if I would send to them a copy of my presentation. I said, well, I don't normally write it up, but I prepare slides and I can send you the slides. So, I did.

Well, lo and behold, I received back a paragraph from the American Society for Microbiology and they would like to endorse my presentation. So, this is the first endorsement I have ever had of my presentation.

[Laughter]

DR. DOYLE: So, I'm going to read to you this endorsement.

The American Society for Microbiology endorses my presentation today and would like to commend the administration for focusing on the problem of microbial, food-borne disease and emerging pathogens. ASM is the largest single life sciences society in the world, with over 42,000 members. Many ASM members are engaged in the research, detection, diagnosis, prevention and surveillance of food-borne disease.

Research and the public health infrastructure related to food safety needs to be strengthened and funded appropriately. ASM supports increased attention and federal funding to address the complexity and magnitude of the problems associated with food safety.

So, I thank ASM for that endorsement.

[Laughter]

DR. DOYLE: I'm not going to get into specific microbiological tests for detection of food-borne pathogens, but rather talk about issues or gaps that are associated with a variety of these tests. In essence, there are similar common gaps or problems with most if not all of these tests. I'm going to give you a listing here of the various factors, if you will, that are associated with microbial testing and we have gaps linked to each of these areas.

I'm going to address sampling, enrichment, which involves the recovery of injured cells, the detection test itself, isolation procedures, enumeration, pathogenicity testing, real time, reduced time assays and genetic fingerprinting. That sounds like a lot, but we're going to do it in 20 minutes. So, hold on.

Sampling methodology, this is probably one of the most critical points in microbial testing. Often times, microbes are non-homogeneously distributed in foods and what we need to do is, to be able to detect small numbers of highly infectious microorganisms in very large volumes of foods in which the organism may be non-uniformly distributed.

There are two examples, I think, that are timely and at the forefront right now for the types of foods for which we do not have good tests or sampling procedures to detect pathogens. One is alfalfa seeds. Several outbreaks recently have been reported associated with E. coli 157 and Salmonella that go back to seeds, alfalfa seeds. I can't tell you how many hundreds of pounds to tons of alfalfa seeds have been tested associated with these outbreaks and they still haven't been

able to isolate E. coli 157 or Salmonella.

Another example is raspberries. Guatemalan raspberries have been implicated in more than one outbreak here in the U. S. and Canada. We still don't have a test that will enable us to detect Cyclospora raspberries. It is likely that we have small numbers of these pathogens present in the food or in the seeds and they are not uniformly distributed. So, how are we going to test our sample appropriately to pick up these pathogens?

Well, we need methods that will actually concentrate these microorganisms from very large volumes of foods. Preferably, these tests should be non-destructive. I'm talking idealistically here now, but an example is testing poultry.

We use rinses, where we put the poultry carcass into a wash and we can rinse the entire carcass. Then we can concentrate those cells with immunobeads and there are other approaches to immunoconcentration or concentration today.

Also, we should have concentrators that don't bind other microorganisms besides the target organism. This is a problem in immuno- concentration whereby other bacteria that are not wanted can also bind to the beads beyond the target cells.

Another important point in sampling methodology is, methods are needed to detect these non-homogeneously distributed pathogens. I think the best example that we have are these large combos of meat that are used to prepare hamburger. How do we go about getting a representative sample when it may be just one little cut of meat within this one ton of meat that is contaminated? Well, one approach may be using the exudate, the liquid that comes off of the meat and collects at the bottom.

Another example is sampling sprouts. How do we sample sprouts, vegetable sprouts this is, for E. coli 0157? Well, one thought is, we are continually putting water into these large growing chambers and we may take the water that comes out of the bottom of these growing chambers and test that for the pathogens.

The next stage within the system of microbial detection is enrichment. Enrichment is largely used to pick up the injured cells that often are present in foods that are processed.

Many of the methods, the rapid tests that we have today, require that large populations of the target microorganism be present in order for these systems to be effective in detecting the microorganism. Hence, in order to get these populations up to 10^5 per ml or whatever the minimum levels are for that particular test, we have to go through an enrichment procedure so that we can pick up that one cell in 25 grams or whatever the test limit may be.

The enrichments necessary, as I mentioned, to resuscitate injured cells and to get that target organism to grow up to the numbers that are needed for detection, what we need are reduced time and enrichment procedures that will stimulate the growth of the injured--well, recovery of the injured cells as well as the growth of the target organisms and suppress the

background bacteria that are often present in very large populations on foods. This is no easy feat.

The clinical microbiologists can't believe why we are having such difficulties as food microbiologists in picking up pathogens in food. The reason is, because we, as food microbiologists, have millions, in many cases, of other bacteria to compete with these few cells of harmful bacteria that may be present in the foods. So, the purpose of enrichment is important. This is largely a major limiting factor in developing truly real time, rapid tests for detecting pathogens.

Now, the detection methods themselves, what are some of the important criteria for these detection methods. Well, first of all, they need to be sensitive. The bottom line depends on the criteria set by regulatory agencies. In many cases, it is one cell in 25 grams. With meat, ground beef, it is increased. For E. coli 157, I think it is one cell in 300 and some grams now.

Another important point is, it has to be accurate and sensitive. We don't want a lot of false positives; we don't want a lot of false negatives. I'd say, less than one percent is a reasonable level, but ideally we want to get down to zero false positives, zero percent false negatives.

As we heard before, it has to be affordable. We have to have a test that costs less than $10 to be competitive.

It has to be easy to perform. For example, we don't want to have to have a Ph.D. in order to run the test in the lab. Ph.D.'s will get tired of running routine tests after a while. In fact, in many processing facilities where we have routine tests being done, it is high school graduates that are performing these tests. So, it has to be a test that is very easy to use.

Ideally, the test should be rapid, at most, one day. We have tests out there that are one day, preferably, less than eight hours. If you can't do it in one day, don't do it in 12 hours, because that's too long for a shift or for a person to be doing that kind of a test. You have to do it in an eight-hour day or less. Preferably, it is real time.

Now, I want to talk about two types of assays. These are two of the common types of assays that are out there. One is immunoassays, immuno-based assays. These are usually based on antibodies that will bind specific antigens to the target organisms.

Now, the pros of these types of assays is that they are easy to perform and they are affordable. You can usually get tests like this for $10 or less. The cons are, you will often get unacceptable levels of false positive results. You will get a positive result for Salmonella and you go through and confirm it later and it is not Salmonella. So, you have a product that is highly perishable like precut lettuce or hamburger, you want to move that product. You can't contend with many false positive results.

Now, what we need is increased specificity in these tests. So, we can have some assurance that, if it comes up positive by the immunoassay, yes, that is contaminated with

Salmonella or whatever that target organism is and make a decision based on that. We need these assays to be real time, if at all possible. When I say real time, I'm talking less than 15 minutes to get a result.

The next slide should address PCR methods. These assays are largely based on gene sequences to specific targets to the microorganism of interest. The pros are that, they can be highly specific and quite definitive. So, if you get a positive result by the PCR assay, you can make some decisions and say, yes, that really is Salmonella that we are detecting and then withhold that product, reprocess it or whatever else needs to be done.

The cons are that, at least, today these tests are not any quicker than the immunoassay-based tests or any other rapid test and there can be complications associated with these PCR-based tests. If there are certain enzymes in the food, like raspberries, that compete with some of the enzymes used in the PCR test so that you don't get a sensitive assay.

The real need with PCR-based tests is what they talk about, but can't come through with. That is, they need real time tests, something you can run in 15 minutes and have an answer.

DR. DOYLE: Let me talk about the last slide we have on detection methods. No, we're going the wrong way, I think.

What we really need to do, especially for emerging pathogens is, be able to develop detection procedures that will detect small numbers of these emerging pathogens. Some good examples are the parasites, like Cryptosporidium and Cyclospora and even Helicobacter pylori. We know this organism is an important cause of gastric ulcer, but we don't know where they're coming from, how they are transmitted. There is some suggestive evidence that they may be coming or transmitted through water and perhaps certain foods.

The next category has to do with isolation methods. Why do we need to isolate pathogens after we have presumptively detected them? Well, there are a couple of reasons. One is, we need to confirm that the pathogen truly is the target organism, like Salmonella, especially in immuno-based assays, where we may have a relatively high occurrence of false positive results.

The second reason is, we may want to further characterize that organism genetically so that we can do some genetic fingerprinting that will enable us to see if that organism may be associated with outbreaks or for other purposes.

Now, what do we need in the area of isolation methods? Well, first of all, we need to better enable the growth of microorganisms, preferably all of the cells of the target organism.

So, what do we need? We need to ideally, if we develop the optimum isolation method, we need a medium that will enable the growth of the target organism, preferably all of the cells of the target organism, which would include the injured cells. We need to restrict the growth of the unwanted organisms. Often we have to apply antibiotics and other selective agents to enable us to do that. Ideally what we need is one isolation medium that could pick up all the harmful

microorganisms within one group.

For example, Salmonella and E. coli 0157 and some of the other enterics, if we could just put that sample on that isolation medium and see different colors or whatever, we could isolate the pathogen of interest.

All right, that then brings us to the enumeration methods. So, we have talked about isolating the organism. Now, we also may want to know how many harmful bacteria are present in a food.

Well, there are some real difficulties encountered here in terms of enumerating small numbers of microorganisms in foods. We do, again, have to contend with the issue of recovery and enumeration of these injured microorganisms. We have to be concerned about the growth of the normal cells in the presence of selective agents. This is an issue that is often overlooked.

If 95 percent of a target organism like Salmonella will grow in the presence of a certain antibiotic, well, then that antibiotic may be added to the selective medium, but it will miss. You will miss five percent of the Salmonella that won't grow in the presence of that antibiotic.

The third point is that we have to restrict the growth of the competitive microorganisms. No matter how good the growth medium is in recovering the injured cells, it is not going to help if the competing bacteria overgrow the plate.

Why do we need enumeration procedures? Well, if our regulators, in their best judgment, some day come up with some tolerances for certain pathogens in foods, such as Listeria, which some countries do have these criteria where they will tolerate a hundred Listeria per gram, Listeria monocytogenes per gram in certain foods. Then we need an enumeration procedure that will enable us to pick up a hundred Listeria monocytogenes per gram, possibly Campylobacter.

There are some investigators who suggest numbers of Campylobacter may be more important than just detecting Campylobacter in a food. Campylobacter is a bit unusual compared to some of the food-borne pathogens in that, it doesn't grow in foods normally. So, if it gets down to a few cells of Campylobacter, which is below the infectious dose, do we need to be concerned about those foods?

The other purpose for doing these enumeration studies is to do fate and activation studies. We need to define what the appropriate conditions are to eliminate pathogens from foods. Right now, we don't have enumeration procedures that will enable us to enumerate Cyclospora or perhaps Cryptosporidium in foods. So, we need to develop these.

Pathogenicity determination is another very important point. We need to be able to differentiate the human pathogens from those bacteria that may fall in the same species, but are not pathogenic to humans. An example is the enterohemorrhagic E. coli versus the shiga toxin-producing E. coli. If we were today to say, hey, we can't have any more shiga toxin-producing. coli in ground beef, we would be in trouble, because surveys suggest up to 20 or more percent of

ground beef is contaminated with sugar toxin-producingE. coli.

What we need to focus on are those strains of enterohemorrhagic E. coli, which are a subclass of the shiga toxin-producing E. coli. We know those are human pathogens. So, we need a test that will enable us to fish out or separate the enterohemorrhagic E. coli from the shiga toxin-producing strains.

Also, there is evidence to suggest that, there are highly virulent strains of Listeria monocytogenes and weakly virulent or perhaps avirulent strains of Listeria monocytogenes. We need an easy test to sort those types of bacteria out as well.

Ideally, we would like to have real time tests, tests that in some cases might be used in a HACCP system, whereby we see results in seconds or minutes after a food has been processed and we can run that test and make a correction based on the results of that test. There are some biosensors that look very promising, that will enable us to give results within a matter of minutes.

I'll give you just one example here, this integrated optic interferometer that was developed at Georgia Tech. It was developed for other purposes, not for microbial testing, but for testing certain constituents in air. They have used that technology in microbial testing and they find that they can pick up as few as ten to the third Salmonella per mil in a matter of minutes. It is expensive in that, they only have a single use format and it would have to be perfected.

This is an example of an area that shows real potential, these biosensors.

I mentioned genetic fingerprinting. These have some real benefits. The CDC has used pulse field gel electrophoresis fingerprinting to identify outbreaks, where they have peaks and unusual fingerprints of bacteria, pathogens that they then go back and track back to what food was actually the source of the pathogen and outbreak.

Another valuable reason for doing this type of fingerprinting is to determine the sources of undesirable microorganisms in processing plants and foods. You might find that you have Listeria in your end product and then you go test the plant and you find that you have Listeria all over the plant. If you can fingerprint those strains, you might find that there is one dominant strain in the product and there is one strain that matches that in one area in the plant. That is the area that is really giving you the fits.

What do we need to do in terms of improving these methods?

Well, first of all, some of these methods are not very discriminatory. For example, pulse field gel electrophoresis is very good for E. coli 0157 and CDC has adopted that as the gold standard for testing genetic fingerprinting of 0157. When you use it to test Salmonella typhimurium DT104, you get one common band basically for all the strains of DT104.

Ribotyping, another example, is a good method for Listeria monocytogenes. There is a very limited number of profiles for E. coli 157.

These tests are not inexpensive and they take a long time to run in some cases. Now, the

pulse field gel electrophoresis test for 0157 has been reduced from several days to one day, but still we hope it can be reduced to a shorter time at less cost.

Okay, the final comment. Microbiological testing is not a sole solution to eliminating the risk of transmitting food-borne pathogens. However, it can be a useful adjunct to the overall food safety net. So, let's keep in mind that we are not going to eliminate our problems with microbial testing even if we have that ultimate real time test and the best sampling procedures available. We are not going to eliminate it.

We have to take all sorts of approaches, as those have been discussed today, from farm all the way to the fork.

So, I thank you for your attention.

DR. ELLIS: Thank you, Mike. I'm sort of reminded of the similar incident you had in Indiana a few months ago when the power went out.

Our next speaker is Dr. Elsa Murano from Texas A&M University. She will probably talk to you a little bit about the new technologies, which probably include irradiation.

New Technologies

DR. MURANO: I want to tell you that my presentation was sponsored by the American Society for Slide Projectors. So, we will see; we will see what happens.

I'll try to make this sort of brief, since we have had to go over time. I know you folks are tired and hungry. So, we will see what we can do.

I was coming back from Honduras about three weeks ago, before the storm hit, thank goodness. I was reading, I think, it was "Newsweek Magazine" and there was this report, this article: "Safer Food for a Tastier Millennium." It was an article that talked about how it seems like the next step in the evolution of food science is to develop foods that are very tasty, very good for you, healthy, nutritious, but that they are safer.

In that article, they talk about irradiation, UV light processing and all types of technology. So, I thought, boy, what an appropriate article for me to find. So, I thought I would show that to you. I don't pretend to know what the media thinks or says.

If we consider any kind of a decontamination or intervention strategy--and new technologies is what I'm here to talk to you about. You can consider that there are probably more than this, but I came up with about eight elements that are important in trying to figure out what the success of those particular strategies might be. So, this is applicable to whatever strategy you want to think about.

First of all, obviously, it has to be able to reduce or even eliminate the food-borne pathogens that are your target. It has to be able to do that without damaging the quality of the product, without reducing the shelf life and hopefully, will enhance the shelf life of the product. Consumers have to accept it. It cannot be something that consumers would never buy and we are

going to touch on a little bit of that when we talk about food irradiation.

Certainly, above all, it has to be safe. It has to be a safe process or a safe method that produces foods that are wholesome and safe to eat.

The cost versus the benefits, obviously, the benefits should outweigh the costs. It is very important for the practical application of any technology. Hopefully, it is a technology or an intervention strategy that can complement other strategies as well, in order to really put the hurdle effect into practice.

Ideally, it would be a technology that would be applicable to a myriad of products, but even if not, certainly that would have product applicability, for the products that we need to be decontaminated. Then it would be--for the success of any technology, it has to be logistically feasible. We are going to talk about some of that in just a second.

So, I could have talked about all kinds of new technologies. I say new, quote-unquote, because some of these are not so new. I chose these five technologies, because they are technologies that have been studied to some degree or another, but yet not everything is know about them for us to be able to successfully apply them, to decontaminate food. So, I'm going to touch on steam pasteurization, pulse light or high-intensity visible light, UV light, high hydrostatic pressure and ionizing radiation.

I want to point out that, all of these have been deemed safe by regulatory agencies. If we consider, for instance, ionizing radiation, which may be the most controversial of the ones on this list, it certainly has been approved by the FDA. After looking at numerous studies throughout the years, it has been endorsed by the World Health Organization, on and on. I don't have to convince you, I think, about that fact.

So, when I started to think about this presentation and to decide what technologies to talk about, certainly, preharvest, we have discussed it much and I'm glad because I'm not going to talk about any strategies that are used preharvest, but rather the slaughter processing part. Further processing is where we can see the application of these five technologies that I'm going to talk to you about today.

Steam pasteurization, visible light, UV and ionizing radiation all can be applied at the slaughter processing floor as well as further processing. High pressure, high hydrostatic pressure is more applicable as a further processing technology.

So, let's look at those eight elements again. This time I put them as a series of steps here towards obtaining safer food. You have the safety of the technology, the effectiveness, the quality of product after that technology has been applied, how applicable or to what products it is applicable, effect as a combination in several strategies that are applied, the logistical issues, cost benefits and then consumer acceptance or acceptability. When you consider all of these, regarding each of these technologies, we need to then figure out which of these steps are missing

for each of these technologies.

So, what do we know and what do we need to know?

I don't want to bore you and tell you all about these technologies, what they are all about and so forth. We don't have time anyway, I wanted to just touch on a few little things that we certainly do know. They are the basis for me choosing these technologies to talk to you about.

Effectiveness, certainly one of the most important basic elements of the success of a technology. So, I have listed here the five technologies and the highest percent reduction of bacterial load that you would find in food by applying this technology. Here I give you the parameters.

You can see that steam pasteurization, you can get one or two log reduction or 99 percent. Visible light gives you only about a log. UV light gives you a couple. The hydrostatic pressure gives you a couple at this level, but when you combine high pressure with heat, which can be done very easily, simultaneously when you use this technology, you can achieve a whole lot of reduction with this technology. Ionizing radiation, same thing.

It all depends on the levels that you use. You can really reduce the number of microorganisms in a food, depending on the level of the process that you use.

So, we talked about effectiveness. Now, when we address quality, applicability and the use of a technology in combination with others, that is where we start to see a few gaps.

Steam pasteurization, pulse light, UV light, high pressure, ionizing radiation, they all have quality issues with them. These can be minimized, depending on the type of parameters that you use. With steam pasteurization, there is a concern that there is a color change.

That can be minimized and so forth, but I can tell you that, in Texas, we had a group of Mexican industry people visiting. They wanted to go to plants that had one of these steam pasteurization units, because they were concerned that the meat that they were purchasing had a different color to it, had been discolored by this technology. So, they wanted to see for themselves whether it was this technology that was doing it and what anybody was doing about it to minimize those changes.

Certainly, it is applicable to carcasses. There has been some work done on combinations with organic acid rinses and hot water rinses and so forth.

High intensity light, certainly the color and the odor can be affected. You can minimize that by keeping the level of the pulses very low and you can apply it to carcasses and cuts. There has been, again, some work done on combining it with other treatments. As you saw in the previous slide, the reductions are not very great. So, this is a technology that I'm not sure is going to really go too far.

UV light, the quality has been studied and you can pretty much control any changes, as far as what people who have done research in this area have told me. Combinations with other

strategies haven't really been addressed very much. That is something that we need to look at.

High pressure processing, I've done a lot of work in this area and can definitely tell you that the color and the texture change. You put a piece of chicken in one of these pressure units or a piece of meat and it will be a partial cook, no question about it. It tenderizes the product as well. So, obviously it changes the product that it is no longer "a fresh" product, but it certainly can have its use and its application.

We have done some work with the simultaneous application of heat.

Ionizing radiation, not only can you control the quality changes, but there has been, I beg to differ with Dr. Girdhar, but there has been a lot of work done on the effects of irradiation and the quality of meat products. You can apply it not only to cuts, but also to ground product, which is certainly very useful.

A lot of these technologies, when you look at pulse light or UV light, which are similar in terms that it is an energy source that you are applying to the food, they are only able to penetrate the very top surface of the product. Whereas ionizing irradiation can go through the product. So, you can decontaminate ground meat very easily.

With regard to the effect with other combination treatments, you know, people have looked at it under lab conditions in terms applying heat before or after radiation and so forth, but we haven't really looked at it in terms of what happens to cuts or to ground product that comes from a carcass that was steam pasteurized. How low of an irradiation dose can you give it, because you had steam pasteurized the carcass before?

Logistics, capital costs and acceptability by consumers, you can see there, I got these figures from the different manufacturers of equipment. They are only approximations, so don't hold me to these. Don't call them up and say, hey, Elsa Murano said, no more than 150,000.

Logistically speaking, steam pasteurization, pulse light, UV light, these are technologies that basically you have some kind of a chamber that a company can install on the premises. When you talk about high pressure and ionizing radiation, that may not be quite true, especially with ionizing radiation. It is a lot more complicated than that. It depends on what thickness of material you need to process, whether you need to have thick concrete walls and a separate building or whether you can just a unit at the end of the line.

Do you need to ship your product to a contract irradiator, for instance? So, logistical issues enter into it.

Consumer acceptability of steam pasteurization; I don't think anybody has done a study on consumer acceptance, but I don't think that is necessarily a concern, because it is a heat treatment. But pulse light and UV light, I don't know if there would be any concern from consumers if they knew that they had just purchased a piece of meat or some other product that was treated with ultraviolet light. Maybe they wouldn't care, but I haven't seen any studies done on these issues.

I wouldn't expect there to be any problem with high pressure either. Ionizing irradiation, I put a question mark and a check mark at the same time, because there continues to be a controversy over whether consumers will accept irradiated products or not. Many studies have been done to show that consumers would accept irradiated products, but other studies are not so positive.

The real test of any of these technologies is to just put it in the market and let people choose. They will choose with their pocketbook. Don't worry about that.

So, if we had to make a list of the kind of more precise things, more detailed items that need to be studied about all of these intervention strategies, you might think of these two types of areas. Number one, besides the studies that have been done in terms of effectiveness, what other factors can influence that effectiveness? If there is a lot of organic matter on the surface--and let's say we are talking fruits and vegetables that haven't really been washed very well, because somebody says, hey, I'm going to treat this with UV light or I'm going to treat this with that matter, does that matter?

How much organic material is on that surface in terms of affecting how that intervention strategy kills those microorganisms. Does the surface have a lot of moisture or fat? What is the temperature or pH of that surface, the texture?

These things don't matter with some of these technologies, but for instance with UV light and visible light, they do matter. The smoother the surface, the more effective these methods are. So, that immediately starts to suggest, if we knew the answers to all these question, we would be able to say, for this product and that product, we can use these technologies. So, we can start to target to the different technologies to optimize conditions as best we can.

On packaging parameters, B. K. Girdhar made a mention of modified atmosphere packaging. Studies have been done, at least, in food irradiation on the use of modified atmosphere packaging, but there are a few little questions that we still have to figure out, because some people have shown that, depending on the gas you have in there, you could have more or fewer survivors. So, we still have little details to work out in some of these technologies.

Then what foods can be used with all of these technologies?

Whole muscle versus ground? Does the species matter, meaning the type of tissue, does it matter?

In the case of vegetables and fruits, does it matter - the type of surface and some of the other properties of those specific foods? Can seafoods be used in all of these technologies? Does the quality get affected so much that you can't really use any of these technologies?

So, these are some of the factors that we have to consider, issues and research that we need to do some work in to fill in the gaps that exist.

When we talk about combinations of strategies, I kind of hinted that there were some

technologies where we had done some work on combining them with other things. Can we combine those strategies in such a way that we optimize their conditions of the stronger microorganisms, but yet don't negatively affect the quality. That is really the key issue.

I can combine many interesting processing methods and really do a number on these micro-organisms, but if it is going to affect the quality, then it is not good. So, we have to look at the hurdle effect. When you have preharvest strategies, how does that, whatever it is that you are doing preharvest, how does that effect the efficacy of the post-harvest strategies and vice-versa? Can you minimize the treatment that you give to foods post-harvest because of what you have done preharvest?

That is the farm-to-table philosophy, if you think about it. What treatments work better before other treatments, the order and the time elapsed from the time you apply one treatment versus the time that you apply the next one? Does that matter? Should they be done immediately or even simultaneously?

The cost benefit analysis is very important and that is usually one of the last things people look at when they are looking at intervention strategies. Consumer attitudes and acceptance, we want to do consumer attitude studies that are real life, that really give you a good answer, that is not just a bunch of people that you educated on a certain technology and, of course, they will accept it because they trust you with the information you gave them. Maybe if they go somewhere else and they don't know anything about the technology then they won't accept it. Maybe they will; maybe they don't care.

There was a study done not too long ago and I heard a scientist from Iowa State University report on it. You had irradiated chicken presented to shoppers at a supermarket in a display case right next to non-irradiated chicken. The irradiated chicken was clearly marked as so. They had a big sign. They had even little brochures that the USDA has designed with the ten most frequently asked questions about food irradiation.

Basically, what it turned out to be was, whichever was cheaper, that's the one people bought. They couldn't care less if it were irradiated or not.

They look at all the different factors. Those people didn't go home and throw out that chicken when they finally read the label. Did they read the label and were making an informed purchase? We don't know.

So, this is our last line. Again the five strategies and again the eight steps.

In terms of safety, we don't really have to do anything else because these are technologies, again, as I've said, that have been approved for use by the U. S. Government, by the FDA. So, we don't have to spend time and money just to redo things and reinvent the wheel, so to speak.

So, when it comes to effectiveness, quality, applicability and combinations, all of the strategies need some work, because we need to, at the very least, not only look at the factors such

as texture and pH and atmosphere and all those things that I mentioned, but we have to be able to use all these technologies and figure out the optimal conditions when these strategies are applied either alone or in combination for not only reducing microbial pathogens, but maintaining the quality as high as possible.

When we get to logistics, irradiation and high pressure processing, we have to do some research in that area to see what would work best for different types of businesses. Cost benefit analysis, all of them have to have that done.

Then consumer acceptance, certainly, the light and UV and certainly irradiation. We need to put to rest this question of whether it is accepted or it is not accepted by consumers. We have to finally put our efforts to answering that question and just put it to bed one way or another. Otherwise, we just keep talking about the same thing time and time again.

I think that was my last slide.

See how the American Society for Slide Projectors, it helped me.

Thank you very much.

DR. ELLIS: Well, we have the last presentation. That is always a dubious honor.

The Organizing Committee is circulating a rumor that you have to get a coupon from Michael after the presentation, before you go to the reception.

[Laughter]

Chemical Treatments

DR. DAVIDSON: Actually, it is just for your first drink.

DR. DAVIDSON: My talk has been endorsed by my mother.

DR. DAVIDSON: She also made my slides.

[Laughter]

I want to thank the Organizing Committee for inviting me today.

I have learned a lot today. One of the most important things I've learned is, I'm going to go back and change my research program to involve manure in some way.

The committee asked me to talk about chemical treatments research needs. That is kind of a broad area. I have to say that, I have worked with food antimicrobials for the past, about 20--well, over 20 years. I have seen a lot of changes, interest by the food industry rise fall, rise again. In fact, we were just having a little meeting, a little reunion in the back of the room, a few minutes ago, before we started this session.

I kind of consider the golden age of food antimicrobials as the time when Monsanto and mostly Mike Robach were doling out all sorts of money to do research on sorbates back in the middle to late 1970s. John Sorbate or John Sofos Sorbate back there was one of the key players in that and Merle Pierson as well. So, did I do all right, Merle? Is that enough?

[Laughter]

DR. DAVIDSON: Okay.

I'm really a firm believer in food antimicrobials and the role they can play, the important role they can play in the delay of growth of both food-borne pathogens and spoilage microorganisms. When you are talking about food antimicrobials, generally, you are dealing with not so much inactivation but simply delay of growth. If you are talking about something like sanitizers, that is where you're talking about killing micro-organisms.

In this age of concern for food safety, these compounds could provide just the margin of safety that a company needs to prevent abuse. I think that is kind of where the difference was, what Elsa was talking about and mine is. Really, with food antimicrobials, I'm looking at kind of the last stage here, how the consumers handle the food products, except for sanitizers, where that is kind of a preprocess condition.

If companies would use some of these antimicrobials, I think that they may not end up on my food poisoning hall of fame slide. If a lot of people didn't consider food preservatives as kind of poisons or toxins, I think some of these logos on products might just not be on this slide.

What I would like to do is cover several areas, the types of chemical antimicrobials. This is where I kind of wanted to define what I'm going to discuss. Antimicrobials added directly to foods, including both traditional antimicrobials and naturally occurring antimicrobials and then a little bit about sanitizers, although I'm going to touch on some of these things and I'm going to go into a little bit more depth in some of the other areas.

Believe it or not, there is really a lack of organized information on the effectiveness of even the traditional antimicrobials, things as simple as their use percentages, their effectiveness in various foods and especially their mechanisms. The function of traditional antimicrobials and naturally occurring antimicrobials is to prolong shelf life and inhibit pathogenic microorganisms.

One of the things, again, I want to note is, most of these things are bacteriostatic. That is, they prevent the growth of the organisms. They are not necessarily bacteriocidal. There are cidal compounds, but the ones that are traditionally known as antimicrobials are often times bacteriostatic.

By inhibiting, these compounds are actually preserving the quality of these products and not hiding spoilage. I think that is something that consumers sometimes don't realize. The compounds will not usually work very well if you have a poor product or a poor quality product or a poor quality ingredient. Eventually, the microorganisms are going to grow. You're going to get pathogens growing and spoilage organisms growing. The higher the initial number, the shorter the shelf life is going to be.

This latter point kind of differentiates these compounds from things like antibiotics. Where you could potentially use an antibiotic to overcome poor sanitation, that is not the case with most of the food antimicrobials.

mgs

The traditional role for sanitizers, I think, was as a method for reducing or killing microorganisms on food contact surfaces. That is how they started out. In the last five to ten years, actually about the last five years, they have become a real important cog in controlling the growth of microorganisms on raw fruits and vegetables and raw meats and poultry.

We have heard several discussions today, I think, about how those things need to be researched more.

These are the research areas that I would like to talk about with chemical antimicrobials. You already saw my last slides, so you know where I'm going to go anyway. What I would like to do is kind of give you an update. These are the areas that I feel are the ones where most of the research is being done at this point in time.

First of all, there are novel types. Really, when you talk about novel types, you're not talking about sorbate anymore. You are really talking about things like naturally occurring antimicrobials. In fact, it is pretty much you don't see too many new types of "traditional antimicrobials." It is all pretty much natural.

We are going to look at combinations of antimicrobials. I kind of feel like that is the best way to apply these things, but there are some problems with that and I'll go through that. The same with packaging, we can apply these compounds at packaging but, again, there are some drawbacks to that.

Finally, I'm going to finish up with a little bit on resistance development.

As far as novel types of antimicrobials go, I think--well, for example, Dale mentioned using propionic acid in animal feeds. Well, that would be kind of along those same lines. Most of the research has gone out of that area and looking for new sources.

Sanitizers are a little different because things like chlorine dioxide, ozone, peroxyacetic acid, all those need to be studied as far as their effectiveness, especially in raw fruits and vegetables and poultry and meats. So, there is a lot of room for sanitizer work in that area, because we really don't know what the effectiveness of those compounds are, especially in various commodities.

Again, the hot area really is naturally occurring antimicrobials.

There are really three areas where you can find naturally occurring antimicrobials, animal sources, plant sources and microbial sources. The animal sources, just to give you some examples, include things like the lactoperoxidase system. In milk, which inhibits gram-negatives, lysozyme which occurs in milks and eggs, which has just been approved as a food additive. So, I guess we can put it on the traditional list. It does degrade the cell walls of gram-positive bacteria.

Lactoferrin, which is an iron-binding compound which we showed when I was at the University of Tennessee that--by the way, I'm at the University of Idaho, not Washington State University. I forgot to mention that. Idaho is not Ohio. It's not Iowa. It's Idaho.

Lactoferrin, which is a compound that we studied at the University of Tennessee, which we showed to inhibit the growth of Listeria monocytogenes in a milk system, which was a pretty good finding. The only problem was, it was fairly high concentrations of the compound that it took to inhibit the growth of the organism.

Probably bigger than animal sources or plant sources, there is just a wide variety of compounds. You have heard about all these people going out in the world and looking for compounds that can be used as human drugs from plants in the world. There are a lot of people doing the same thing, looking for compounds that can be used as inhibitors in foods. Some of the old ones include spices and essential oils, allium-based or sulfur-based compounds from garlic and onions.

One of the promising groups or, at least, one of the individual compounds is alloisothiocyanate and its use as a vapor has shown some real promise in both antimicrobial systems and in food products and also phenolics and phytoalexins. So, there are a number of potential sources there.

If you look at naturally occurring antimicrobials from microorganism sources, we have the old kind of traditional, regulatory-approved compound nisin, whatever way you want to pronounce. The compound is produced by Lactococcus lactis, subspecies lactis and also natamycin, which is also a regulatory-approved compound on cheeses. It is produced by Streptomyces natalinsis [ph].

There are really a ton of other compounds that have been isolated as "bacteriocins" or antimicrobials from lactic acid, bacteria and related organisms. All these things show a different spectrum and very, very few of them have actually been applied to food products.

One potential exception to that is a compound that is produced by Pediacoccus, called pediacin. That has been shown in some food systems to work fairly well.

I want to talk quickly about the research needs for natural antimicrobials. I'll mention that at the end as one of my top five research needs. There are so many things with natural antimicrobials, I want to kind of talk about it right here.

First of all, looking at the activity of the compounds, there is, again, a ton of these newly discovered things. I highly suggest that, if you want to read about naturally occurring antimicrobials in foods, that you get a copy of this book called Naturally Occurring Antimicrobials in Foods, that was published by CAST, the Council for Agricultural Science and Technology, about six months ago. The lead author is Dr. John Sofos. I did help him a little bit, but not very much.

In that, we cover the types, how you might apply them, et cetera.

Now, getting back to this, since we have a lot of these newly discovered compounds that are often times applied or used against single organisms, there really needs to be a lot more work

done on the spectrum of activity of those compounds. Even more importantly, it seems to be a hobby of a lot of researchers to isolate these things and say they might be used for--useful for foods, in inhibiting pathogenic organisms, but then they never do that.

So, probably 99 percent of them, have never actually been applied to a food product. What happens often times is, that when you apply these things to a food product, you lose a lot of the activity.

I think that when they first started isolating bacteria, since they discovered that fairly quickly, that it was going to be the magic bullet and then somebody decided they were going to put into a food product and it didn't work very well.

The other thing is that isolating antimicrobials from plant sources; there are a lot of people who want to isolate them and then they are kind of organic chemist types and they want to purify, purify, purify. I highly recommend that they don't do that. I think that the best way to apply these things would be as the crudest possible extract that you can get.

Let's face it. What would you rather have, watermelon extract on the label or some big, long, hairy, organic chemical on your label. So, if the things can't work as a fairly crude extract, I don't think that they are going to be very useful.

If they are going to purify these things, they need toxicological data and then that gets pretty expensive, because they have to have that before they can get regulatory approval. Things like economics then come into it. Again, all those things will contribute as to whether these things are approved or not.

Another one that I didn't even have were sensory properties.

The second area is antimicrobial combinations. This is an important research area at this point in time. A lot of times, I get questions and people say, well, how do you run combination studies. Well, unfortunately, there is not exactly a rule of thumb for running combination studies. It's pretty much trial and error.

Because we don't know much about the mechanisms of food antimicrobials, we can't sit there and say, well, I'm going to choose this one because it acts in this way and then I'm going to choose this one because it acts this way. One of the areas that we need a lot of work on is the mechanisms of the food antimicrobials that we have.

A way to look at using antimicrobial combinations is not only combinations of two compounds, but with processing methods, such as, the non-thermal methods that Elsa mentioned. In fact, for high pressure processing, they are already using things like sorbate and benzoate in combination with those.

Then an area that, surprisingly, I have seen very little done with is, looking at antimicrobials in combination with heat. What I want to do is just show you a little study that we did that encompasses some of those areas.

mgs

First of all, we wanted to look for an antimicrobial that would work fairly well against E. coli 0157:H7 and we were kind of looking at this in terms of, well, could we use it in ground beef. We used three strains, 43895, WSU 4 and KSU 3 and we applied or we added .5 mM EDTA, first of all. It had no effect on the organisms. One percent sodium lactate had no effect. If you added EDTA and sodium lactate together, it had no effect.

Monolaurin, which is a monoglyceride with lauric acid as the fatty acid on it, at 25 micrograms per ml, inhibited one of the organisms. If we put all three of them together, we could completely inhibit all the organisms. There were some aspects of this that showed that we could potentially get some synergistic activity with this combination.

Notice that we did it in a tryptic soy agar. So, this was done in antimicrobial media, pH6, because we were trying to match somewhat the pH of the ground beef.

So, what we wanted to do was actually apply this stuff to ground beef and, hopefully, provide a safety factor during heating. So, the next step we wanted to do was, what effect these compounds had on the heat resistance of the organism. This is the D_{55} values for the combination of organisms in peptone which is, again, a microbiological media.

With just monolaurin and EDTA at 100 micrograms per ml each, you can see that for the control, the D values or somewhere between 20 and 25 minutes. Whereas, with the antimicrobials, the D_{55} values were about two minutes. So, we actually reduced the D value by about one log with those antimicrobials in there. So, it's pretty effective.

Then we did the thing that everybody seems to kind of forget to do and that is, apply the things to the food product. I know from past experience that, when you do that, you're going to lose a lot of your activity.

This shows you the D_{60} values for one of those strains, the 0157:H7 in ground beef, with all three of the compounds this time, monolaurin, EDTA and lactate and bumped up in concentration to 1,000 milligrams per kilogram of monolaurin, 500 of EDTA and one percent sodium lactate.

This time, in the control, the D value was 0.79 minutes. With the antimicrobials, it was 0.47 minutes. So, instead of getting a one log decrease, we did cut it about half. There was a significant difference. So, therefore, we feel like we have shown that this might be a way that you can add a safety factor to the cooking of ground beef if it were slightly undercooked.

In other areas, antimicrobials in packaging, there are combinations with modified atmosphere packaging. That is one way to go, using, say, volatiles in a package like alloisothiocyanate, where you add it and it is an effective antimicrobial. There are some things that the Japanese are doing by putting in sachets that produce ethanol in packages and the ethanol is an inhibitor. So, there are two ways you can do it. Actually, that is more like controlled atmosphere packaging.

Using incorporation of antimicrobials, you can put it on the surface. In fact, that has been around since 1945, when they put sorbate on the surface of packages, one of the first uses for sorbate. Now days, you can put it into the films. I'm sure you have heard of those antibacterial cutting boards that contain triclorsan. You can do the same thing. You can put triclorsan in films.

You can put chlorine dioxide in films. There are a lot of potential areas you can go with this.

The big drawback with packaging is that, the only organisms you really affect are on the surface of the product. If that is your major problem, then that's great. If it isn't, then if you are trying to package a whole chicken, I don't think that is going to work very well.

The last area I wanted to mention was resistance development. Again, when we talk about antibiotic resistance, I guess, it just kind of brings up the thought of, what about food antimicrobials. Are we having problems with that as far as resistance development?

Well, if you look at approved food antimicrobials, the traditional ones--I went back and I looked in the literature and I did find some information on using sorbate and benzoid as far as their potential resistance development. There really isn't any. No matter how many times they exposed organisms to these things, they got very little increases or any acquired resistance to either benzoate or sorbate. So, there's not a real big problem there.

The same with sanitizers and disinfectants. I mean, let's face it. We have been using the things for close to a hundred years. I figure if we had a big problem with that, somebody would have figured it out a long time ago.

Naturally occurring antimicrobials, on the other hand, are a little bit different, especially the microbial types. It has been shown in a number of studies since the 1980s that, you do get a resistant population of microorganisms, say, when you apply nisin to a population. It is like about one and 10^7 and 10^9. It has been shown with both Listeria monocytogenes and Clostridium botulinum.

There are some really good studies. In fact, Tom Montville, a graduate student and, Allison Crandall at Rutgers have done some outstanding research on identifying why that happened. They did show that the microorganism does change and is actually a resistant organism.

The scenarios though for developing resistance and having that be a problem with this type of compound are pretty remote. You have to have some type of continuous exposure of the organism to the antimicrobial. Besides, nobody really is using these things as a total method for control of a pathogen in a food product anyway. So, it is probably not a great problem, but it is something that still needs some investigation.

Another question that we have asked before is, what is the interaction of antibiotic

resistance and resistance to process factors. Then the last area--I'm going to cover that in a second. The last area is stress protection.

There could be a whole talk in stress protection. It has been shown in the last five or ten years that, if you expose a microorganism to stressor, such as, pH or temperature, the microorganism can become more resistant to subsequent stresses, such as, pH. I think Dale talked about that a little bit, you know, where you the pass the microorganism. If E. coli sees a low pH, the next time it sees a low pH, it is going to be even more resistant.

Obviously, you know, a long way to go on that and it definitely needs to be researched more.

Just one question that I don't think anybody every really seems to ask. That is, do antibiotic-resistant cells have increased resistance to other environmental factors or to food antimicrobials?

The reason I started asking that is, I see things like Salmonella typhimurium DT104 and you kind of go, why is this thing hanging around? What is it about the organism that makes it tougher? Nobody really looks at that, that part of it and tries to compare it.

We did a study a couple, three years ago where we just took some strains of antibiotic-resistant and non-resistant Salmonella cells and did some heat resistance studies with them. We did actually a number of studies, including their growth at 25^{o}C, freeze resistance, effective pH and heat resistance.

Generally, there were no differences until we got to the heat resistance part. I will say that we did two other cultivars, Heidelberg and typhimurium and saw some trends towards higher heat resistances with antibiotic-resistant cells, but not a significant difference. However, when we looked at Salmonella enteritidis, we saw about twofold higher heat resistance, at 55 degrees C for the antibiotic-resistance strains versus the non-antibiotic resistant strains.

Again, this is a very limited study. It may not mean anything, because we may have just picked the strains. I don't know. I would kind of like to see a larger study done where there were some comparisons with the environmental resistance of the two types of organisms.

Okay, my top five. These are in priority order.

I think the first thing that needs to be done and would be an ideal thing for USDA, especially somebody like the Eastern Regional Research Center to do is, look at the mechanism and action of traditional antimicrobials. We talked about basic research. This is pretty basic stuff, but if we are ever going to be able to apply food antimicrobials intelligently, based on their mechanisms, rather than just pulling their names out of a hat, we have to know more about how they work.

Secondly, is the impact of resistant development. All those areas I mentioned, I think, need to be looked at, even more on the traditional antimicrobials. Obviously, the naturally

occurring ones are going to have to be looked at as they come into the fold.

Natural antimicrobials, I already covered all the areas that I think need to be done there.

Combinations based on mechanisms, that, of course, depends on number one and then looking at maybe better, more effective uses in packaging.

Thank you again for the invitation.

Discussion of Papers

DR. ELLIS: Well, I hope the quality made up for running over. I certainly appreciate the audience staying with us.

Dr. Girdhar commented that he might have to leave early. I'm not sure if he has left already. Anyway, if we can have the remaining speakers come up here and we will take a few questions before we go to our evening refreshments.

[Pause]

DR. ELLIS: Are there any questions?

[No response]

DR. ELLIS: I guess you are off the hook.

Again, I'd like to give all the speakers a hand for some excellent presentations.

[Applause]

[Whereupon, at 5:15 p.m., the proceedings were recessed to be resumed, at 8:00 a.m, Friday, November 13, 1998.]

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